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"The Batteries of Internal and External Enemies Will Be Constantly and Actively—Often Covertly and Insidiously—Directed against Your Political Fortress. Watch Over Its Preservation with Jealous Care!"—George Washington.

Vol. XXVII, No. 6 JUNE, 1938

JOURNAL
OF THE
AMERICAN PHARMACEUTICAL ASSOCIATION

TRADE MARK

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THE 86th ANNUAL MEETING OF THE AMERICAN PHARMACEUTICAL ASSOCIATION WILL BE HELD IN MINNEAPOLIS, MINN., Hotel Nicollet, August 22–27, 1938.

The 1938 Meetings of the American Association of Colleges of Pharmacy, the National Association of Boards of Pharmacy, Conference of Pharmaceutical Association Secretaries, of the Pharmaceutical Law Enforcement Officials and the Plant Science Seminar will also be held in Minneapolis, Minn.

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GENERAL PROGRAM FOR THE EIGHTY-SIXTH ANNUAL MEETING OF THE AMERICAN PHARMACEUTICAL ASSOCIATION AND RELATED ORGANIZATIONS, NICOLLET HOTEL, MINNEAPOLIS, MINNESOTA, AUGUST 21–27, 1938.

AUGUST 15TH–19TH.

Plant Science Seminar.

SATURDAY, AUGUST 20TH.

2:30 P.M. National Conference Pharmaceutical Research.
6:30 P.M. Dinner, N. C. P. R.
8:30 P.M. Evening Meeting, N. C. P. R.

SUNDAY, AUGUST 21ST.

9:30 A.M. Council, A. PH. A.
8:30 P.M. American Council on Pharmaceutical Education.
9:00 P.M. Opening Concert.

MONDAY, AUGUST 22ND.

9:00 A.M. A. A. C. P.—Executive Committee.
9:30 A.M. Chemistry Conference.
Pharmacy Conference.
Pharmacognosy and Pharmacology Conference.
Pharmaceutical Economics Conference.
9:30 A.M. N. A. B. P.
1:00 P.M. Luncheon and Style Show (Ladies).
1:30 P.M. A. A. C. P.
1:30 P.M. N. A. B. P.
6:30 P.M. Joint Dinner, N. A. B. P. and A. A. C. P.
8:00 P.M. A. A. C. P.
8:30 P.M. First Session, Conference Pharmaceutical Law Enforcement Officials.

TUESDAY, AUGUST 23RD.

9:00 A.M. Sightseeing Trip to St. Croix Falls, returning via River Road, Luncheon (Ladies).
9:30 A.M. Joint Conference, A. PH. A., N. A. B. P. and A. A. C. P.
2:00 P.M. N. A. B. P.
2:00 P.M. A. A. C. P.
6:30 P.M. Dinner, Rho Chi Fraternity, followed by Annual Meeting.
8:00 P.M. First General Session, A. PH. A.
10:30 P.M. Smörgåsbord and Entertainment.

WEDNESDAY, AUGUST 24TH.

9:30 A.M. First Session, House of Delegates, A. PH. A.
12:30 P.M. Luncheon (Ladies), followed by a meeting of the Women's Auxiliary of the A. PH. A.
12:45 P.M. Luncheon, Committee on Syllabus.
12:45 P.M. Luncheon, Kappa Psi Fraternity and Lamba Kappa Sigma Sorority.
12:45 P.M. Luncheon, Phi Delta Chi Fraternity.
2:30 P.M. Council, A. PH. A.
2:30 P.M. First Session, Scientific Section.
2:30 P.M. First Session, Sub-Section on Pharmacognosy.
2:30 P.M. First Session, Section on Education and Legislation.
2:30 P.M. First Session, Section on Practical Pharmacy and Dispensing.
2:30 P.M. First Session, Sub-Section on Hospital Pharmacy.
2:30 P.M. First Session, Section on Historical Pharmacy.
2:30 P.M. First Session, Section on Pharmaceutical Economics.
2:30 P.M. First Session, Conf. Pharm. Assn. Secretaries.
3:30 P.M. Meeting, Committee on Nominations.
3:30 P.M. Meeting, Committee on Resolutions.
6:30 P.M. President's Reception.
7:30 P.M. Joint Banquet, A. PH. A. and Related Organizations.

THURSDAY, AUGUST 25TH.

9:30 A.M. Second General Session, A. PH. A.
12:00 M. Luncheon for Honor Guests.
12:00 M. Luncheon—Kappa Epsilon.
12:15 P.M. Veteran Druggists' Luncheon.
1:30 P.M. Sightseeing Tour—University, College of Pharm., Minnehaha Falls, Lake Minnetonka, etc.
6:00 P.M. Dinner.
8:30 P.M. Second Session, House of Delegates, A. PH. A.

FRIDAY, AUGUST 26TH.

9:30 A.M. Joint Session, Scientific Section and Section on Practical Pharmacy and Dispensing.
9:30 A.M. Second Session, Sub-Section on Hospital Pharmacy.
9:30 A.M. Joint Session, Section on Education and Legislation, Conf. Law Enforcement Officials and Conf. Pharmaceutical Assn. Secretaries.
10:30 A.M. Breakfast (Ladies).
12:15 P.M. Special Luncheons.
2:30 P.M. Card Party (Ladies).
2:30 P.M. Second Session, Scientific Section.
2:30 P.M. Second Session, Section on Education and Legislation.
2:30 P.M. Second Session, Section on Practical Pharmacy and Dispensing.
2:30 P.M. Second Session, Section on Historical Pharmacy.
2:30 P.M. Second Session, Section on Pharmaceutical Economics.
2:30 P.M. Second Session, Conf. Law Enforcement Officials.
2:30 P.M. Second Session, Conf. Pharm. Assn. Secretaries.
6:30 P.M. Dinner, Former Presidents, A. PH. A.
7:30 P.M. Meeting, Committee on Resolutions.
8:00 P.M. Final Session, House of Delegates, A. PH. A.
10:30 P.M. Farewell Dancing Party.

SATURDAY, AUGUST 27TH.

9:30 A.M. Final General Session, A. PH. A.
1:00 P.M. Council, A. PH. A.

EXECUTIVE COMMITTEE FOR THE 1938 AMERICAN PHARMACEUTICAL ASSOCIATION CONVENTION.

Top Row: L. to R.: E. B. Fischer, Chm. Northwest Branch, A. PH. A.; C. V. Netz, Local Treasurer, A. PH. A.; Henry Moen, Chm. Banquet Committee; Abe Strimling, Chm. Registration Committee; Frank Moudry, Executive Committee; Jesse B. Slocumb, Executive Committee; William Peters, Executive Committee; Oscar Nordrum, Chm. House Committee. Bottom Row: William Kregel, Chm. Finance Committee; Jack Harms, Chm. Reception Committee; E. J. Prochaska, Publicity Committee; Henry H. Gregg, Jr., Executive Committee; Hallie Bruce, Executive Committee; Dean C. H. Rogers, Local Secretary and Convention Chairman; Mrs. Frank Moudry, Ladies Committee; Henry C. Kruckeberg, Executive Committee; Walter Fields, Chm. Entertainment Committee.

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

VOL. XXVII JUNE, 1938 No. 6

MINNESOTA PHARMACISTS PREPARE FOR ALL-TIME HIGH IN NATIONAL DRUG CONVENTIONS!

When the defenders of the public health, the American pharmacists, converge on Minneapolis from every nook and corner of the continent in August, they will be accorded a welcome and hospitality that is being prepared right now by their Minnesota colleagues. Every druggist in the "Land of the Sky Blue Waters" is putting in double time at this early date maturing plans for entertainment, recreation and inspiration.

The pharmaceutical Conferences, Sessions and Seminars, which will step up the humanitarian service of the profession, will attract the foremost pharmacologists in the nation. The Executive Committee for the 1938 AMERICAN PHARMACEUTICAL ASSOCIATION Convention, headed by Dean C. H. Rogers of the College of Pharmacy, University of Minnesota, and the pharmacy leaders of Minneapolis and St. Paul, are all at work with the goal definitely set for a convention that will prove an all-time high. Their meeting at the University, Wednesday, June 15th, resulted in the maturation of plans which are truly ambitious.

The nation itself is interested in the August Minneapolis convention owing to the fact that out of the pharmaceutical research conferences, education, pharmacognosy and illicit drug law enforcement discussion, great public health benefits will undoubtedly accrue. The foregoing sessions, which will run daily throughout the convention week, will be of intense interest, not only to the attending pharmacists but to the entire world of pharmacy.

The beautiful Nicollet Hotel of Minneapolis will be the hub of conference, banquet and dance. From its doorways eleven of Minnesotas ten thousand lakes can be reached within 15 minutes—and all of them large enough for fishing, sailing and canoeing.

The Chairman of the Entertainment Committee, Walter Fields, has already plotted a fifty-mile scenic tour to the historic St. Croix river country and the primeval Indian country of Taylor's Falls. There is no tour in America so quaintly beautiful, passing through the Swedish village of Lindstrom, along the banks of the Chicago chain of lakes onward to the Interstate National Park. Therein flows

E. J. Prochaska, Publicity Committee; Henry H. Gregg, Jr., Executive Committee; Hallie Brice, Executive Committee; Dean C. H. Rogers, Local Secretary and Convention Chairman; Mrs. Frank Moudry, Ladies Committee; Henry C. Kruckeberg, Executive Committee; Walter Fields, Chm. Entertainment Committee.

one of the most unique rivers in America, the famed St. Croix. This body of water is almost one hundred per cent pure and is chock full of river pike, sunfish and the gamest fighting fish in any waters, the small-mouthed black bass. Fishermen come from all over the world to catch these bass.

A special treat for the ladies, beside the St. Croix River Tour, is a Style Show and Luncheon which is to be staged in the Terrace Lounge of the Nicollet Hotel. The creations in milady's charm habiliments will be modeled from the dress designers of Paris, London and New York.

A striking cuisine novelty for every one has also been scheduled—a genuine Swedish smörgåsbord which only those who have visited Stockholm restaurants can adequately describe for its great gustatory goodness. The Swedes are artists in many fields, and particularly so in the preparation of unusually tasty dishes of which the smörgåsbord has won international acclaim.

The climax of joy and beauty will be the ball at the conclusion of the convention which will be held in the grand ballroom of the hotel. Special lighting, air conditioning, finest orchestral music, flowers and refreshments will set the atmospheric framework for this event.

These are but specimen flashes of the plans already being set by the Minnesota pharmacists in preparation for the convention week in August. Nationally known speakers, outstanding in pharmacological achievements are already booked to address Seminar and Conference. Among these will be Dr. Robert L. Swain, President of the National Association Boards of Pharmacy, and Dr. Hugh C. Muldoon, President of the American Association of Colleges of Pharmacy, world recognized writers on pharmaceutical subjects and brilliant crusaders in the cause of public health. In the same heights will be the President, Dr. E. N. Gathercoal, and other prominent speakers, who will play outstandingly major rôles in the convention.

Minnesota is proud of the honor America's pharmacists have conferred upon her in staging the 1938 convention in its "City of Sky Blue Lakes." Her defenders of the public health, the entire profession of pharmacy, will leave no stone unturned to make this convention a mile-stone in pharmaceutical history. The therapeutics of the Pharmacopœia, will, in the North Star State, be augmented by the analgesic of Minnesota's giant forests, lakes and woodland havens.

CONTRACT FOR HALL OF PHARMACY SIGNED.

A lease was signed June 25th between the Fair Corporation and Show Globe, Inc., under which the latter gets possession of the Hall of Pharmacy in the New York World's Fair to open in 1939. The rental will be $322,778. The building contains 23,027 square feet of exhibit space, and is situated on the Court of Power, a short distance eastward from the Theme Center.

Space in the Hall of Pharmacy will be sublet to companies and organizations of the drug industry, and the project undertaken by Show Globe, Inc., contemplates an expenditure of approximately $1,000,000. Nearly a score of manufacturers are reported to have indicated their intention to participate in the exhibit, which will comprise every phase of the drug industry from crude materials to finished products, as they go to the consumer.

Details of the exhibits have not yet been completed.

EDITORIAL

E. G. EBERLE, EDITOR 2215 Constitution Ave., WASHINGTON, D. C.

A. PH. A. LABORATORY.

WHEN plans were developed for the Headquarters Building in Washington, provision was made for three newer activities for the ASSOCIATION to develop, a Reference Library, an Historical Museum and a Research Laboratory, the latter to be devoted to the establishment and improvement of standards for the official drugs and medicines. The Library and Museum have been in operation for some time. With the opening of the A. PH. A. Laboratory on June 15, 1938, the third unit was put into operation.

The official standards have now become so numerous and exacting and so important from the legal as well as the public health point of view, as to require the most accurate facilities and control in their development. The recent enactment of the new Food, Drug and Cosmetic Act makes this movement all the more important and necessary. While the National Formulary and the Recipe Book, being the property of the ASSOCIATION, will receive primary attention in the Laboratory, it is expected that the research program will be widened so as to contribute more extensively to the revision of the U. S. Pharmacopœia.

At the 1935 Meeting of the ASSOCIATION in Portland, Chairman Gathercoal of the Committee on National Formulary, which was then about to complete the Sixth Edition, stated that if the necessary studies in connection with adequate Formulary revision were to be properly carried out, a laboratory should be established promptly where much of the control work could be handled. It was recommended that a temporary N. F. Laboratory be established in the School of Pharmacy, University of Illinois, where adequate facilities were offered to meet the pressing revision demands and to provide experience in operation before the permanent Laboratory was opened in Washington.

The N. F. Laboratory was opened in Chicago under the direction of Chairman Gathercoal, about January 1, 1936, and met an almost instant and pressing demand for the solution of many revision problems following the issuance of the Sixth Edition of the National Formulary in December 1935. During this period, 123 assignments have been made of which 87 have been completed, and 33 subjects are as yet unassigned.

At the 1936 meeting of the A. PH. A. in Dallas, Chairman Gathercoal reported the successful operation of the Laboratory and recommended that it be transferred to Washington as early in 1938 as possible. Later, a Committee with Dr. Gathercoal as the Chairman, was named to develop general plans for the Washington Laboratory.

These plans were approved at the New York meeting in 1937, the necessary appropriations were made and the Committee was continued to prepare the rooms, equip the Laboratory and transfer the personnel, records, materials, etc., from the Chicago Laboratory to Washington. The preparation of the rooms was completed in March, according to the floor plan, page 456, and they have since been equipped with laboratory furniture of the latest design and with the necessary apparatus and supplies.

Work in the new Laboratory opened on June 15th with the arrival from Chicago of Dr. Roy K. Snyder and Messrs. Emerson C. Beeler and Karl B. Rosen, who have been connected with the work for some time. Mr. Kenneth L. Kelly, who is research associate in the National Bureau of Standards, under grants from the N. F. and the U. S. P. on the color problem, will also be connected with the Laboratory. Dr. Gathercoal will continue to serve as Director during the year.

Recently the Council of the ASSOCIATION elected the following as members of the permanent Committee on Laboratory to have general supervision of its activities: George D. Beal, *Chairman*, Carson P. Frailey, Charles B. Jordan, John C. Krantz, Jr., and Joseph Rosin; with Chairman Cook of the U. S. P. Committee of Revision, Chairman Gathercoal of the Committee on National Formulary and Chairman Lascoff of the Committee on Recipe Book as ex-officio members. This Committee held its first meeting in Washington on Tuesday, June 21st, took over the charge of the Laboratory from the previous committee and adopted plans for its activities. All projects for investigation in the Laboratory or through outside grants will be submitted to the Committee through the ex-officio members and all reports on work done will be issued through the Committee in order that the program may be thoroughly coördinated and controlled. The Laboratory will be enlarged in personnel and equipment as experience indicates.—E. F. K.

PROPOSED PLAN OF STUDY OF MEDICAL CARE.

THE STATE and county medical societies are being encouraged by the American Medical Association to undertake studies to determine medical needs and to formulate preferable policies for supplying these needs in accordance with established policies and local conditions. The objectives of the study are classified as follows:

First: To determine the prevailing need for medical and preventive medical services where such may be insufficient or unavailable.

Second: To discover and to remove, if possible, the obstacles which interfere with the more efficient distribution of medical services.

Third: To develop a frank and friendly exchange of information on the demand and supply of medical and preventive medical service.

Fourth: To urge that information be kept up-to-date in each community, thus enabling the professions and other responsible agencies to maintain the local demand and supply of medical and preventive medical services in constant balance.

The state and county medical societies have been advised to contact various agencies, including pharmacists, which are most likely to have data concerning medical needs. It is therefore logical to suppose that when these societies begin the surveys of existing facilities they will set up committees which will include representatives of all agencies able to supply necessary information.

State pharmaceutical associations and county and local associations will certainly be contacted and it is essential that full coöperation shall be forthcoming in this very important undertaking. Pharmacists who have definite knowledge of local health conditions and who are therefore competent to work with committees of physicians and other professional and lay persons working on this serious problem should be selected to serve if requested.

The Committee on the Study of Pharmacy of this ASSOCIATION has been working with the Bureau of Medical Economics of the American Medical Association in formulating the questionnaire and the schedule of information to be obtained from pharmacists. Copies of the questionnaire and information about the study have been sent to the state pharmaceutical associations with the request that they contact their state medical society, with an offer of assistance, and also inform their county and local associations. Obviously, it is to the interest of the public health professions to show the extent of services now being rendered by them both to private patients and to the indigent, and that they can meet all reasonable demands for additional services.

Actual facts and figures are necessary if an equitable procedure for supplying medical care is to be worked out in the interest of the people as well as the professions. The practice of pharmacy is naturally affected by all changes in the present method of providing medical services. Pharmacists have a very great interest in this situation and should coöperate fully and wholeheartedly with those who are endeavoring to get the facts and, then, to develop a procedure based on these facts.—E.F.K.

TRI-STATE HOSPITAL ASSEMBLY.

This Assembly, sponsored by the Hospital Associations of Illinois, Indiana and Wisconsin, was held in the Stevens Hotel, Chicago, May 4–6, 1938. One of the nineteen sections of the Assembly was the Conference of Hospital Pharmacists which held three sessions on May 4th and 5th, under the able chairmanship of Dean C. B. Jordan of the School of Pharmacy, Purdue University.

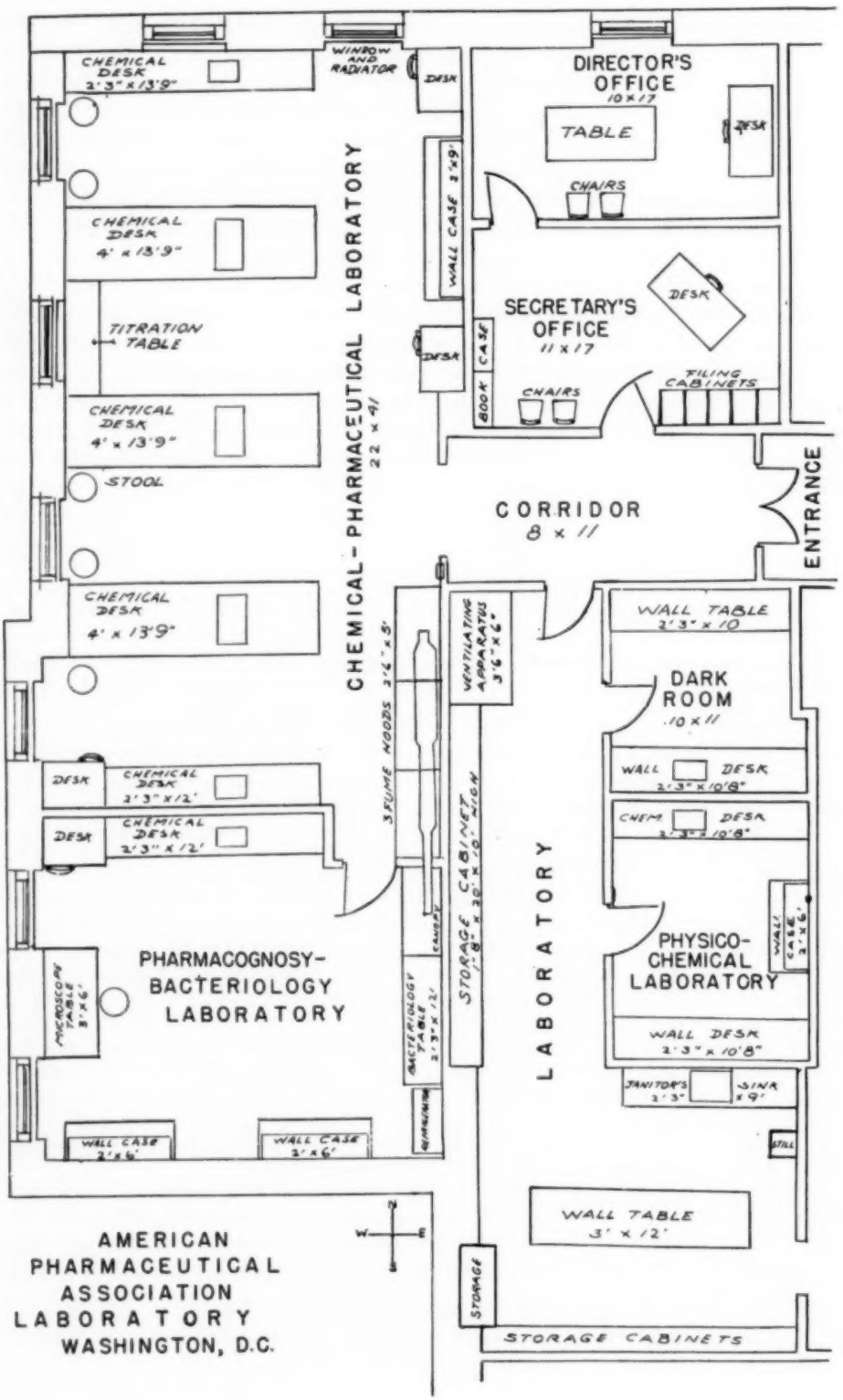
The following papers were presented during the two morning sessions:

1. Report of Chairman, C. B. Jordan. 2. "Systematized Services by Hospital Pharmacists," P. M. Clair, Jackson Park Hospital, Chicago, Ill. 3. "Hospital Formularies," Sister M. Stephanina, St. Elizabeth's Hospital, La Fayette, Ind. 4. "The Drug Formulary in Our Hospital," Beatrice A. Zeman, Women and Childrens Hospital, Chicago, Ill. 5. "Problems of the Hospital Pharmacist," S. W. Morrison, Illinois Research and Educational Hospitals, Chicago, Ill. 6. "Coöperation of the Pharmacist with Internes," Fred R. Berger, Indiana University Hospitals, Indianapolis, Ind. 7. "The Therapeutics Committee of the Hospital," Bernard Fantus, Director of Therapeutics, Cook County Hospital, Chicago, Ill. 8. "The Pharmacist's Services to the Physician," Charles W. Strout, Grant Hospital, Chicago, Ill. 9. "The Pharmacists' Activity in the Navy," F. G. Lyon, Chief Pharmacist, U. S. Navy. 10. "Opportunities of Hospital Pharmacists Serving in Other Professional Capacities," Mary Dienhart, Methodist Hospital, Rockford, Ill. 11. "The Modern Pharmaceutical Curriculum," C. O. Lee, Professor, Purdue University, School of Pharmacy, La Fayette, Ind. 12. "New Medicinals," Elizabeth K. Neufeld, University of Chicago Clinics, Chicago, Ill. 13. "Suggestions for Manufacturing Pharmacy in Hospital Dispensaries," H. G. DeKay and C. O. Lee, Professors, Purdue University, School of Pharmacy, La Fayette, Ind. These papers have been filed with the A. PH. A. and are available to anyone interested.

The afternoon session on May 4th was devoted to an Administrative Panel Round Table Conference on Hospital Pharmacy Problems which was very helpful.

An instructive pharmacy exhibit was included among the Educational and Technical Exhibits, under the auspices of the AMERICAN PHARMACEUTICAL ASSOCIATION, and the School of Pharmacy, Purdue University. This exhibit included a collection of hospital formularies which will be preserved in the AMERICAN INSTITUTE OF PHARMACY and will be available for future exhibits of this type.

The Hospital Pharmacists' Section of the Tri-State Hospital Assembly will be continued under the direction for the next year of S. W. Morrison as *Chairman* and Elizabeth K. Neufeld as *Secretary*.


CHEMICAL DESK 2'3" X 13'9"
WINDOW AND RADIATOR
DESK
DIRECTOR'S OFFICE 10 X 17
TABLE
CHAIRS
WALL CASE 2'X9'
CHEMICAL DESK 4' X 13'9"
SECRETARY'S OFFICE 11 X 17
DESK
TITRATION TABLE
CASE
BOOK
CHAIRS
FILING CABINETS
CHEMICAL DESK 4' X 13'9"
CHEMICAL-PHARMACEUTICAL LABORATORY 22 X 41'
STOOL
CORRIDOR 8 X 11
ENTRANCE
CHEMICAL DESK 4' X 13'9"
3 FUME HOODS 2'6" X 5'
VENTILATING APPARATUS 3'6" X 6"
WALL TABLE 2'3" X 10'
DARK ROOM 10 X 11
DESK
CHEMICAL DESK 2'3" X 12'
WALL DESK 2'3" X 10'8"
CHEM DESK 2'3" X 10'8"
DESK
CHEMICAL DESK 2'3" X 12'
STORAGE CABINET 1'8" X 32" X 6'-9" HIGH
LABORATORY
PHYSICO-CHEMICAL LABORATORY
PHARMACOGNOSY-BACTERIOLOGY LABORATORY
MICROSCOPE TABLE 3' X 6'
BACTERIOLOGY TABLE 2'3" X 12'
CABINET
WALL CASE 2'X6'
WALL DESK 2'3" X 10'8"
JANITOR'S 2'3"
SINK 1'X 9'
WALL CASE 2'X6'
WALL CASE 3'X6'
STILL
WALL TABLE 3' X 12'
AMERICAN PHARMACEUTICAL ASSOCIATION LABORATORY WASHINGTON, D.C.
STORAGE
STORAGE CABINETS

SCIENTIFIC SECTION

BOARD OF REVIEW OF PAPERS.—*Chairman*, F. E. Bibbins; H. M. Burlage, W. G. Crockett, E. V. Lynn, C. O. Lee, L. W. Rising, L. W. Rowe, Heber W. Youngken, Ralph E. Terry, Carl J. Klemme.

A PHYTOCHEMICAL AND PHARMACOLOGICAL INVESTIGATION OF TRILLIUM ERECTUM.*,**

BY DONALD C. GROVE,[1] GLENN L. JENKINS[1] AND MARVIN R. THOMPSON.[1]

Trillium has long been recognized as a medicinal drug and is still retained as an official drug in the sixth revision of the National Formulary. The Fluidextract of Trillium is one of the ingredients of Compound Elixir of Viburnum Opulus, which according to the "Prescription Ingredient Survey" of 1931–1932 (1), was prescribed 2.9 times in every 10,000 prescriptions. Despite the fact that the drug is still used to a fair extent, it is surprising to note that very little is known of its chemical composition and physiological action. If Trillium is to remain as an official drug, certainly something conclusive should be learned of its chemical composition and physiological action. It was with this in mind that the present study was undertaken.

The first chemical examination of Trillium seems to have been made by E. S. Wayne (2). He reports having found gum, resin, extractive, tannic acid, starch, a little volatile oil and a principle analogous to saponin, which has been called "trillin" or "trilline," the two terms being synonymous. Millspaugh (3) claims he has corroborated Wayne's analysis in full.

D. J. Prendergast (4) in an analysis of *Trillium Erectum* found it to contain 6% of moisture, 2.3% ash, 8.2% of fixed oil, 4.8% of resin and 18.9% of alcohol extractive. He also reported that there was present a white, amorphous powder, soluble in chloroform. This powder he found was bitter at first and afterward sweetish to the taste. It turned red with hydrochloric acid and purple with sulfuric acid, was insoluble in ether and produced considerable foam upon agitation with water, in which it was quite soluble. From these scant experiments he concluded that the principle must be convallamarin ($C_{24}H_{44}O_{12}$). He also reported having found gum and small quantities of organic acids, but obtained negative tests for alkaloids and volatile oil.

V. I. Reid (5) from an analysis of the drug concluded that beside the usual plant constituents such as starch, tannin, resin and gum, it contained a small quantity of fixed oil and saponin to the extent of 4.86%. He also claimed to have isolated a crystalline acid material soluble in ether. This principle was colored purplish brown by strong sulfuric acid and light green by sulfuric acid and a crystal of potassium dichromate. He suggested that this principle probably resulted from a decomposition of the saponin.

---

* Presented before the Scientific Section, A. PH. A., New York meeting, 1937.

** Abstracted in part from a thesis by Donald C. Grove, presented to the graduate faculty of the University of Maryland in partial fulfilment of the requirements for the degree, Doctor of Philosophy, June 1937.

[1] University of Maryland, Baltimore, Md.

EXPERIMENTAL.

Two different lots of the powdered drug were purchased from a reputable dealer and analyzed immediately after the shipment was received for moisture, ash and soluble extractives according to the general directions and procedure given by the U. S. P. X. The results obtained are given in the following table:

	Per Cent.			
	Drug Lot 1.			Drug Lot 2.
	A.	B.	Av.	A.
Total ash	10.88	10.74	10.81	4.15
Acid-insoluble ash	9.63	9.50	9.57	0.85
Moisture (corr. for vol. const.)	5.20	5.17	5.19	5.36
Vol. ether-soluble ext.	0.81	0.83	0.82	0.88
Non-vol. ether-soluble ext.	7.17	7.19	7.18	8.55
Alcohol-soluble ext.	21.16	19.90	20.53	26.93
Dilute alcohol-soluble ext.	15.90	15.80	15.85	34.86
Water-soluble ext.	12.90	13.10	13.00	26.52
Petroleum benzin ext.	5.32	5.92	5.62	7.98

From the above results it can be seen that drug lot 1 contained a considerable portion of dirt (sand) as shown by the high acid-insoluble matter. Drug lot 2 was apparently a much better lot of drug and gave higher results on extractive matter.

Fifty grams of drug were extracted successively with various solvents. The extracts were dried at 100° C. and weighed. The average results obtained are given below, the solvents being used in the order named in the table.

Solvent.	Drug Lot 1, Per Cent.	Drug Lot 2, Per Cent.
Petroleum ether	5.70	6.19
Ether	0.87	3.54
Chloroform	0.73	0.64
Ethyl acetate	3.98	2.68
Alcohol	19.80	20.14
Water	6.90	...

PETROLEUM-ETHER EXTRACT.

For the purpose of a more complete examination a larger quantity of the drug was extracted with petroleum ether. In the case of drug lot 1, 9.5 Kg. were extracted in a Lloyd Extractor. Twelve kilograms of drug lot 2 were percolated in a large glass percolator. In the case of drug lot 2, as the first percolate was drawn off and diluted with more petroleum ether, an insoluble resin separated out. This resin was apparently dissolved by the fatty oil in the first percolate which was very thick and upon further dilution with petroleum ether separated out. This resin was separated and only the petroleum-ether soluble material examined as fatty oil. The oil from drug lot 1 having been extracted in the Lloyd Extractor contained this resin in solution. Drug lot 1 yielded 539 Gm. of fatty oil, representing 5.66 per cent of the crude drug; drug lot 2 yielded 697 Gm. of fatty oil, representing 5.81 per cent of the crude drug.

The oils from both lots of drugs were a dark reddish brown color with a greenish fluorescence and an odor similar to that of the drug, indicating the presence of some volatile oil. Both oils on standing at room temperature deposited a solid crystalline material. The oils were easily soluble in absolute, 95 and 90 per cent alcohol. They were also soluble in ether, chloroform, carbon disulfide, carbon tetrachloride and benzene. They were insoluble in water.

The following constants were run on the oils:

Specific gravity at 25° C.	0.9005	0.9205	Unsaponifiable matter	4.48%	1.31%
Refractive index at 25° C.	1.4722	1.4677	Acid value	115.5	142.8
Saponification value	205.3	207.9	Acetyl value	92.1	.....
Iodine value	87.3	106.4	Total volatile acid value	9.7	....

The high acid value would indicate that the oil had either undergone hydrolysis in the process of extraction or had already been broken down in the drug and, instead of consisting of triglycerides, now consisted of di- or monoglycerides and free fatty acids. This fact is borne out in the case of the oil from drug lot 1 by the high acetyl value and low volatile acid value. This would also explain why the oils are soluble in alcohol.

A few drops of the oil when spread on a glass slide and left exposed to the air for a period of three weeks, had the same consistency and appearance at the end of this time as before, indicating that it was a non-drying oil. This is in agreement with the iodine value.

The high saponification value and low volatile acid value would indicate the presence of myristic or lauric acids.

A preliminary examination for fatty acids was conducted as follows: after saponification of a portion of the oil and removal of the unsaponifiable matter, the solid and liquid fatty acids were separated by the usual lead-salt-ether method. The solid fatty acids were resolved into two fractions by fractional crystallization from alcohol. One fraction melted at 61.2° C. and the other at 57° C. A 0.2-Gm. portion of the fraction melting at 61.2° C. was neutralized with tenth-normal sodium hydroxide, 7.75 cc. being required. This neutralization value gives a molecular weight of 250.81. The molecular weight of palmitic acid is 256.26. Thus it was concluded that the substance melting at 61.2° C. was palmitic acid. The crystals melting at 57° C. are probably a mixture of palmitic and myristic or lauric acids.

The liquid acids separated by the lead-salt-ether method gave an iodine value of 117.4 indicating the presence of unsaturated fatty acids other than oleic.

The unsaponifiable matter remaining from the saponification of 100 Gm. of the oil from drug lot 2 (amounting to about 1.7 Gm.) was examined as follows: the material was dissolved in hot alcohol and allowed to cool to room temperature. On cooling, a white flocculent precipitate settled out. It was filtered off and recrystallized several times from hot alcohol. Finally only about 10 mg. of a white waxy material remained. This material melted at 75° C. A chloroform solution of it did not decolorize a pale yellow solution of bromine in chloroform, showing the product was a saturated compound. It gave negative reactions for sterol by the Salkowski and Liebermann-Burchard tests. This material was undoubtedly a saturated hydrocarbon. As pentatriacontane ($C_{35}H_{72}$) melts at 75° C., it was concluded that it was this substance.

The residues from the separation of the pentatriacontane were combined and steam distilled until about 400 cc. of distillate were collected. The distillate was shaken repeatedly with ether and upon evaporation of the ether 0.2 Gm. of a pale yellow liquid with a pleasant aromatic odor remained. This residue was a small amount of volatile oil and was too small to examine further.

The material non-volatile with steam was further saponified with a small quantity of alcoholic potassium hydroxide in order to remove any traces of unsaponified fatty oil that might still have been present. The unsaponifiable matter from this second saponification was a golden-brown colored oil. It was taken up with hot alcohol and allowed to stand over night. At the end of this time some globules of oil had settled and the supernatant alcoholic solution was decanted off and allowed to stand over night to crystallize. The supernatant alcohol was again poured off and the crystalline material washed with several small portions of cold alcohol. It was then dissolved in warm alcohol and recrystallized several times from this solvent. Finally, a very small amount of a white crystalline substance remained. When allowed to crystallize slowly from alcohol, hexagonal plates were formed. This material was dried at 100° C. and gave a melting point of 130° C. A chloroform solution of the material gave positive Salkowski and Liebermann-Burchard tests for sterol. There was no more material left for further examination; however, the melting point would indicate that it was a phytosterol which melts at 134° C.

All residues remaining from the separation of the sterol were combined and transferred by means of ether to an acetylation flask, the ether evaporated and the residue refluxed with 5 cc. of acetic anhydride for two hours. The warm material was placed in a separatory funnel and allowed to stand over night. Two distinct layers formed, an upper oily layer and a lower layer of acetic anhydride. The oily layer was separated and heated on a steam-bath to remove acetic anhydride. The residue, which was a brown color, was dissolved in ether and transferred to a small distilling flask and distilled. At about 220° C. a few drops distilled over. The distillate was dissolved in ether, placed in a Babcock bottle and the ether evaporated. The residue was

treated with fuming sulfuric acid (6) and after centrifuging, a small globule of oil floated on the surface of the sulfuric acid. As this material was non-saponifiable, could not be acetylated and did not react with fuming sulfuric acid, it must have been a hydrocarbon or mixture of hydrocarbons. It probably consisted of liquid hydrocarbons ranging from undecane to hexadecane.

The acetic anhydride solution remaining after separating the oily hydrocarbon layer was evaporated on the steam-bath to remove the acetic anhydride. The residue was taken up in warm alcohol and cooled in ice water. A trace of precipitate formed; however, it was too small to purify. This precipitate was most likely a sterol acetate.

ALCOHOL EXTRACT.

The marc left from the extraction with petroleum ether was completely extracted in the Lloyd Extractor with ninety-five per cent alcohol. The alcoholic extract after removal of most of the solvent, amounted in the case of drug lot 1 to about 1900 Gm., in the case of drug lot 2 to about 2800 Gm. These extracts still contained a small amount of alcohol and were of a pilular consistency. The following work, unless otherwise stated, will pertain to the extract of drug lot 2.

Isolation and Identification of Sucrose.—During the process of extraction of the drug in the Lloyd Extractor the percolate was drawn off from time to time in liter beakers. After standing for several days while the remainder of the drug was being extracted, some of the alcohol evaporated and a crystalline material separated out in each of the breakers. The dark brown liquid was decanted and the combined crystals washed repeatedly with small portions of boiling alcohol. The crystals were dissolved in a small quantity of water and filtered. The filtrate was evaporated to a thick syrup and the syrupy liquid poured slowly with constant stirring into absolute alcohol. On standing, a fine crystalline precipitate was obtained. This was filtered and the process repeated until about ten Gm. of a white, sweet tasting, crystalline compound were obtained.

An aqueous solution of the crystals did not reduce Fehling's solution. However, after hydrolysis with dilute hydrochloric acid, the neutralized solution gave a heavy precipitate of cuprous oxide with Fehling's solution.

One-half gram of the crystals left no residue on ignition, showing the absence of inorganic constituents.

The crystals were dried to constant weight at 100° C. and 1.37 Gm. were dissolved in water and made up to 25 cc. in a volumetric flask at 20° C. Direct polarization of this solution in a 200-mm. tube at 20° C. gave a reading of +21.0° Ventzke. The calculated reading for pure sucrose should be +21.08° V. This would indicate that the substance was 99.64 per cent sucrose. Twenty cubic centimeters of the above solution were inverted (7). After standing over night the solution was made to 50 cc. with distilled water. A reading of −2.7° Ventzke was obtained using a 200-mm. tube at 20° C. From the readings before and after inversion the per cent sucrose was calculated using the formula in the A. O. A. C. Book of Methods (7). A value of 99.40 per cent was obtained. The inverted solution gave a positive test for ketoses with Seliwanoff's reagent. From the above results it must be concluded that the crystalline material was sucrose.

Steam Distillation of a Portion of the Alcohol Extract.—Seven hundred and sixty-five grams of the extract were steam distilled and the distillate after shaking with chloroform and ether, yielded 1.86 Gm. of a golden-brown oil, with an odor of valeric acid. This residue was dissolved in chloroform, shaken with small portions of 8% sodium carbonate solution and then with several portions of 10% sodium hydroxide solution. The chloroform solution remaining was evaporated and yielded 0.37 Gm. of a volatile oil with an aromatic odor similar to that of the drug. The sodium hydroxide shakings gave a negligible residue, showing the absence of phenols.

The sodium carbonate shakings consisted of a mixture of volatile fatty acids. An attempt to fractionally distil the acids was not successful. The mean molecular weight of the acids was 120.8 when determined from the neutralization value. As these acids had a strong odor of valeric acid, they probably consisted of a mixture of the acids from valeric to possibly caprylic acid.

The mother liquor remaining from the steam distillation was separated by the process of centrifuging and decanting into water-soluble and water-insoluble material. The water-insoluble matter was mixed with sand, evaporated to dryness and powdered. It was then percolated with petroleum ether, ether and benzene. These solvents removed only small amounts of fatty and resinous matter. The powdered mixture was then suspended in water and freed from sand by decantation.

Isolation of a Glucoside.—The aqueous suspension was treated with about 10 Gm. of barium hydroxide, the mixture evaporated to dryness over a steam-bath and powdered. The powder was extracted with four successive portions of boiling alcohol. The alcohol extracts were combined, cooled, filtered and the alcohol evaporated. The residue, which was insoluble in water, was macerated with water containing a little dilute sulfuric acid, filtered and washed well with water, which removed the yellow color. The residue on the filter was allowed to dry spontaneously and was recrystallized many times from alcohol, until a white, crystalline compound was obtained. The crystals were further purified by treatment with hot ether, benzene and chloroform, these solvents removing only negligible amounts of material, which was discarded. The crystals were again shaken with water and a typical saponin foam was produced. The water was filtered off and the crystals shaken with successive portions of water until a foam was no longer produced on vigorous shaking. The crystals were allowed to dry and recrystallized once more from alcohol. In this manner about 3 Gm. of white crystals were prepared. This compound has been given the name "Trillarin."

Properties and Composition of "Trillarin."—This material, when crystallized from ethyl or methyl alcohol, separates in clusters of silky crystals. Under the microscope, they appear as long, flat, rectangular plates; there appear to be no perfect crystals, all apparently being broken at the ends.

The crystals are insoluble in ether, chloroform and benzene. The solubility in ethyl alcohol at 25° C. is 3.49 Gm. per 100 cc.; in acetone 0.99 Gm. per 100 cc. They seem to be slightly more soluble in methyl than in ethyl alcohol. They are slightly soluble in warm ethyl acetate. The crystals are tasteless. When recrystallized from 95% ethyl alcohol, 0.8245 Gm. of the air-dried crystals lost 0.0329 Gm. on drying to constant weight at 100° C., at loss of 3.99%. The anhydrous material is hygroscopic.

The air-dried crystals melted at 197° to 200° C. (uncorr.). The crystals dried at 100° C. soften at about 204° C. and are completely melted at 211° C. (uncorr.). One-tenth gram of the crystals left no residue upon ignition, showing the absence of inorganic impurities. An alcoholic solution of the crystals gave no precipitate with a saturated alcoholic solution of lead acetate or barium hydroxide. A solution of 0.1786 Gm. of the crystals in neutral alcohol gave a permanent pink color to phenolphthalein with one drop of 0.1*N* sodium hydroxide, showing the crystals to be a neutral substance. Both an alcoholic solution and an aqueous suspension of the crystals gave a positive test for carbohydrates by the Molisch reaction. Tests for nitrogen, sulfur, halogens and phosphorus were negative. When a drop of concentrated sulfuric acid is added to the crystals, they turn at first a red-orange color and finally dissolve giving a golden-yellow solution. This sulfuric acid solution of the crystals produces a violet color on standing with a crystal of potassium bromide, a violet color with a solution of bromine in potassium hydroxide and a red color which turns violet on standing with a ferric chloride solution. It is interesting to note that these colors are given by digitalin verum.

An ethyl alcohol solution of the crystals dried at 100° C., containing 0.3863 Gm. in 25 cc. of solution, gave a rotation of −3.6° angular at 22° C. The specific rotation was therefore −116.3. A molecular weight determination using the elevation of the boiling-point method with absolute ethyl alcohol as the solvent, gave a value of 706. Micro combustion analyses on the crystals dried at 100° C. gave the following results: (1) A 5.371-mg. sample gave 3.851 mg. H_2O and 12.066 mg. CO_2. (2) A 4.507-mg. sample gave 3.325 mg. H_2O and 10.094 mg. CO_2. These results indicate the formula $C_{37}H_{62}O_{14}$ which has a molecular weight of 727.47.

	Per Cent Calculated for $C_{37}H_{62}O_{14}$.	Per Cent Found I.	Per Cent Found II.
C	61.03	61.26	61.07
H	8.17	8.02	8.26
O	30.80	30.72	30.67

Hydrolysis of "Trillarin."—The hydrolysis of the glucoside was carried out as follows: 3.0567 Gm. of the crystals dried at 100° C. were dissolved in 150 cc. of ethyl alcohol, 3 cc. of concentrated hydrochloric acid were added and the solution refluxed on a steam-bath for two hours. The alcoholic solution, which had turned slightly yellow during the hydrolysis, was cooled and poured slowly with constant stirring into 500 cc. of water. The mixture was allowed to stand

over night to permit a fine white precipitate of the genin to settle out. The clear aqueous solution was decanted off through a suction filter, the precipitated material washed several times by decantation and finally transferred to the filter and washed thoroughly with water. The precipitate was allowed to dry, dissolved in hot methyl alcohol, transferred to a tared beaker, the alcohol evaporated spontaneously and the residue dried at 100° C. and weighed. The filtrate from the genin was placed in an evaporating dish and heated over a steam-bath until the alcohol was removed and the volume of the solution was about 100 cc. A small amount of genin which had remained in solution had precipitated out and was filtered off and added to the main precipitate. The total weight of the dried genin was 1.6751 Gm. representing 54.8 per cent of the original glucoside.

This genin has been given the name "Trillarigenin."

The filtrate from the genin contained the sugars or sugar split off during hydrolysis.

Examination of the Sugar Resulting from the Hydrolysis of "Trillarin."—An excess of silver carbonate was added to the aqueous solution in order to free it from hydrochloric acid. The filtrate was concentrated to a volume of about 20 cc. and shaken several times with chloroform which removed the yellow color and any last traces of the genin. The aqueous solution was concentrated to a thick syrup and dried over calcium chloride for two days. The residue was taken up with warm alcohol and the sugar precipitated with ether. The precipitated sugar was filtered off, dried over sulfuric acid and powdered. A portion of the powder gave a strong reduction with Fehling's solution. An aqueous solution gave a negative test for fructose or other ketoses with Seliwanoff's reagent. A portion of the powder gave a negative test for pentoses when heated with hydrochloric acid and phloroglucinol. An osazone of the material was prepared and melted at 205° C.

The remainder of the material was treated with 30 cc. of nitric acid, specific gravity 1.15, and evaporated on the steam-bath to a volume of about 10 cc. After standing 24 hours, no crystals of mucic acid had separated. The solution was allowed to stand 24 hours longer and still no mucic acid separated; the volume of the solution was now about 5 cc. This test indicates the absence of galactose.

The nitric acid solution remaining from the mucic acid test was concentrated to a volume of about one cc., five cc. of water added and the solution made slightly basic by the cautious addition of solid potassium carbonate. Glacial acetic acid was then added until the solution gave a strong odor of acetic acid. After standing over night a few crystals had formed. These crystals when examined under the microscope were found to be the characteristic rhombic crystals of potassium bisaccharate.

It was concluded from the above results that the sugar split off during the hydrolysis of "Trillarin" was glucose.

Properties and Composition of "Trillarigenin."—The dry material was macerated with small portions of water to remove any sugar that might have been present and was then recrystallized from methyl alcohol until white crystals were obtained. The compound crystallized from methyl alcohol in shining wartlike clusters, however, when allowed to dry in the air it gave no definite shape when examined under the microscope.

The dried material gave the same color reactions with sulfuric acid, sulfuric acid and potassium bromide, and sulfuric acid and ferric chloride as were observed for "Trillarin." When dried to constant weight at 100° C., 0.2280 Gm. of the air-dried genin lost 0.0042 Gm. or 1.84 per cent. The dry material appeared to be stable in the air. The 100° C. dried material softened somewhat at 190° C. and melted completely at 197° C. (uncorr.). One-tenth gram of the genin when dissolved in neutral alcohol gave no titration with 0.1N sodium hydroxide, showing it was a neutral substance. The specific rotation of the genin dried at 100° C. in ethyl alcohol at 24° C., using a solution of 0.2207 Gm. in 25 cc., was −98.2. Micro-combustion analyses on the genin dried at 100° C. gave the following results: (1) A 3.180-mg. sample gave 2.728 mg. of H_2O and 8.711 mg. of CO_2. (2) A 2.991-mg. sample gave 2.590 mg. of H_2O and 8.180 mg. of CO_2. These results would indicate the formula $C_{25}H_{39}O_4$ which has a molecular weight of 403.31.

	Per Cent Calculated for $C_{25}H_{39}O_4$.	Per Cent Found. I.	II.
C	74.38	74.70	74.58
H	9.75	9.60	9.69
	15.87	15.71	15.73

The following equation may now be written for the hydrolysis of "Trillarin:"

$$C_{37}H_{59}O_{14} + 2\ H_2O \longrightarrow C_{25}H_{39}O_4 + 2\ C_6H_{12}O_6$$

The theoretical amount of "Trillarigenin" formed should be 55.44 per cent. The actual recovery was 54.8 per cent.

It is of interest to mention that some crystals of "Trillarin" were also obtained from the alcoholic extract of drug lot 1. This principle appears to be a normal constituent of the drug.

Saponin.—Lead acetate was added to a portion of the water-soluble material from the alcohol extract but produced only a faint cloudiness. Lead subacetate was then added, the precipitate separated and freed from lead by means of hydrogen sulfide. The lead-free solution was taken to dryness, the residue taken up with alcohol and ether added to the alcoholic solution to complete precipitation. This process of precipitating with alcohol and ether was repeated several times. The dry precipitate was tan colored and produced a typical saponin foam on shaking with water. It readily hemolyzed red blood corpuscles. This material gave some reduction with Fehling's solution, indicating possible contamination with sugars. Further purification of this material will be necessary before analysis.

Attempt to Isolate Convallamarin.—As Prendergast (4) had reported isolating a water-soluble, chloroform-soluble, amorphous principle which he said was identical with "convallamarin," a special search for this substance was made both by the procedure used by him and by several other methods. The results were negative and neither the so-called "convallamarin" nor anything like it could be isolated.

Possible Presence of Alkaloid.—As preliminary tests had indicated the presence of a substance which gave a precipitate with alkaloidal reagents, the following attempt was made to isolate this substance. One hundred cc. of 10 per cent ammonia and 1500 cc. of ether-chloroform mixture (3 + 1) were added to 500 Gm. of drug lot 2, the mixture was shaken frequently for one hour and allowed to stand over night. The ethereal solution was decanted off through a cotton filter into a large separatory funnel. A fresh portion of ether-chloroform mixture was added to the marc, shaken and macerated over night as before. The solvent from the second extraction was filtered and combined with the first extraction. The combined solutions were then shaken with small successive portions of two per cent sulfuric acid. The combined sulfuric acid shakings were made ammoniacal and again extracted with many small portions of the ether-chloroform mixture. The so-called alkaloid did not seem to be extracted completely by the solvent as ten extractions were made and the tenth extract still gave a positive test with Mayer's and Wagner's reagents. The combined ether-chloroform shakings were then washed several times with water to remove any last traces of ammonia or ammonium salts and then were shaken repeatedly with a one per cent hydrochloric acid solution. The hydrochloric acid apparently completely removed this substance as shown by negative tests with Mayer's reagent on the seventh extraction. The combined hydrochloric acid shakings, which were a deep red-orange color, were allowed to evaporate spontaneously to dryness. The residue amounted to 0.11 Gm. or 0.02 per cent of the drug.

The material was soluble in water, somewhat soluble in alcohol and insoluble in ether and chloroform. When examined under the microscope, the material appeared as red needle-shaped crystals. The crystals did not have a bitter taste. Attempts to recrystallize this material to free it from the red color were unsuccessful. When 0.05 Gm. of the material was run through the usual double extraction procedure for the assay of alkaloids, the residue from the final extraction gave no titration with 0.02*N* sulfuric acid. This shows the non-basicity of this material.

As this substance which gave precipitates with Mayer's and Wagner's reagents was not basic, could not be completely extracted with solvents from an ammoniacal solution, had no bitter taste and was physiologically inactive, it was concluded that it was not an alkaloid. It might have been an impure amino acid or some complex coloring principle.

PHARMACOLOGY.

Historical.—Rafinesque (8) claims to have introduced the drug into Materia Medica. It was described as a medicinal in "Henry's Herbal," published in 1812. The earliest therapeutic use of the drug goes back to the time of the Indians, the Indian women using it after parturition (8). The early colonists probably learned of the virtues of the drug through the Indians and increased its uses. Williams (9) cites several cases in which he obtained great and decided benefits with the

drug in menorrhagia and hæmophtysis. He also cites cases in which it was beneficial in scrofulous eruptions. Hubbard (10) claims to have used the drug successfully in hemorrhages. He states: "From the experience I have had I should think the Trillium had a more decided effect in uterine hemorrhage of the passive kind than all other remedies." Du Kate (11) states that in large doses Trillium is emetic, expectorant, diuretic and laxative; in smaller doses it is astringent and possesses great power in controlling hemorrhages and morbid mucous secretions. He gives two cases in which the drug was used successfully in hemoptysis and hematuria.

Some of the many properties that have been proclaimed for the drug are: Tonic, alterative, emmenagogue, antiseptic, etc. It has also been used internally in cases of hectic fever, asthma, catarrhal coughs, diarrhoea and dysentery. Externally it has been used as a cure for carbuncles, ulcers, tumors, etc. It has also been used by the eclectics in conjunction with bugle weed (Lycopus Virginicus) for diabetes.

In spite of the many uses that have been attributed to Trillium there seems to be no satisfactory evidence in the literature that would justify its being used.

Experimental.—For the purpose of a preliminary pharmacological examination, three different lots of the whole drug, each weighing two pounds, were obtained from J. L. Hopkins and Co., New York. About 500 Gm. of a representative sample of the three lots were ground to a number twenty powder. A tincture was prepared from the powdered drug using a menstruum of three parts of alcohol and one part of water. Eight cubic centimeters of this tincture represented one Gm. of the drug.

An assay of this tincture was made on frogs using the mortality curve frog method of Chapman and Morrell (12). It was assayed in terms of the U. S. P. XI reference digitalis powder. By this method the reference digitalis powder was shown to be 16.6 times more toxic than the drug.

The alcohol from 200 cc. of the tincture was evaporated by blowing a current of air over it until the volume was 50 cc. This material was filtered and administered to an anesthetized cat through the femoral vein. One and one-half cc. of the solution, representing 0.75 Gm. of the drug, killed the cat, which weighed 1.86 Kg., within 5 minutes. Another cat, weighing 2.95 Kg., also received 1.5 cc. of this solution and died within 15 minutes.

Another 200-cc. portion of the tincture was evaporated, by means of a current air, to 50 cc. and then diluted with water to 200 cc. An anesthetized cat was given 0.1 cc. of this solution intravenously and a marked lowering of the carotid blood pressure resulted. When the blood pressure had returned to normal 20 cc. of the solution was given orally and 20 cc. rectally and no activity was observed after two hours. However, when additional doses of the solution were again injected intravenously into the same anesthetized cat, a marked lowering of the blood pressure again resulted and when 6.1 cc. had been administered, the cat died. The above experiments were repeated on another anesthetized cat with the same results and 5.7 cc. produced death.

Sixty cubic centimeters of the above solution equivalent to 7.5 Gm. of drug were given orally to a pregnant cat and no action whatever was evident.

The toxicity observed by the frog method and intravenous cat method as contrasted with the negative results obtained by oral administration of massive doses, indicated that the toxicity was produced by an anaphylactoid circulatory shock due to a saponin-like or protein-like substance.

A solution of the glucoside "Trillarin" was assayed by the frog method of Chapman and Morrell (12) and carried to the point where it was less than one one-thousandth as active as ouabain and still showed no action. It was thus concluded that this glucoside was physiologically inactive.

A one to one-thousand solution of the so-called alkaloid gave no action on frogs when injected in doses as high as 0.035 cc. per Gm. body weight of frog. It can be concluded from this result and from the fact that oral administration of massive doses of an aqueous extract of the drug produced no action, that this material was not alkaloidal in character and that the drug contains no active alkaloids.

SUMMARY AND CONCLUSIONS.

A literature review of the chemical and physiological reports on Trillium has been presented.

Results obtained on moisture, ash and soluble extractives on two different lots of drug are tabulated, as well as the results obtained by the successive extraction of the drug with different solvents.

A fatty oil was obtained from each of two lots of drug. A description of these oils is given and their constants compared. The fatty oils consist chiefly of free fatty acids with some mono or diglycerides. The solid fatty acids consist chiefly of palmitic acid, with probably some myristic or lauric acids. The liquid fatty acids have not been examined but the iodine number would indicate other unsaturated acids than oleic acid. A mixture of volatile fatty acids was isolated, which seemed to range between valeric and caprylic acids.

Examination of the unsaponifiable matter disclosed the presence of a solid hydrocarbon, pentatriacontane $C_{35}H_{72}$, liquid hydrocarbons possibly ranging from undecane to hexadecane, volatile oil and a sterol probably phytosterol.

Sucrose was isolated and identified.

A glucoside, which has been given the name "Trillarin," was isolated and its properties recorded. From combustion analyses and a molecular weight determination, the formula $C_{37}H_{59}O_{14}$ was given to this compound. A survey of the literature has disclosed no compound of this formula.

The glucoside upon hydrolysis yields glucose and a genin which has been given the name "Trillarigenin."

The properties of "Trillarigenin" have been recorded and combustion analyses gave the formula $C_{25}H_{39}O_4$. A search of the literature has failed to show a compound of this formula.

The hydrolysis of "Trillarin" may be represented by the following equation:

$$C_{37}H_{59}O_{14} + 2\ H_2O \longrightarrow C_{25}H_{39}O_4 + 2\ C_6H_{12}O_6$$

This glucoside has proven to be physiologically inactive.

A small amount of material was present which gave precipitates with alkaloidal reagents. It was concluded that this material was not an alkaloid and that the positive tests with alkaloidal reagents were probably due to an amino acid or a coloring principle.

A saponin is present but was not isolated in a pure enough state to determine its composition.

A preliminary pharmacological examination has shown that oral administration of massive doses of a de-alcoholized tincture to a pregnant cat had no effect whatever. Both oral and rectal administration to anesthetized cats also had no effect.

Very small doses of the de-alcoholized tincture produced death when injected into frogs or intravenously to cats. It is believed, however, that death is produced in these cases by an anaphylactoid circulatory shock due to a saponin-like or a protein-like substance.

The usual plant constituents such as resin, starch, dextrin mucilage and oxalate are present. The presence of tannin was not established.

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TOXICITY OF PROPYLENE GLYCOL.*

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INTRODUCTION.

During the past several years suggestions have been made that propylene glycol is a suitable solvent for a variety of purposes, pharmaceutical and otherwise. As a result of this interest several papers (1, 2) have appeared in which attention was directed particularly to toxicological studies on this substance. In connection with another investigation involving the use of propylene glycol it was considered advisable to extend some of these studies for the purpose of completing our own data on this subject. Some of the results to be described confirm those of other authors; and some are believed to be new observations not previously described in the literature. The propylene glycol used in these studies was the alpha form (1, 2 propane diol) obtained from the Carbide and Carbon Chemicals Corporation.

Seidenfeld and Hanzlik (1) reported acute fatal doses for propylene glycol when given intramuscularly and intravenously to white rats and rabbits. They also investigated the effects in growing rats of the continued drinking of water containing various amounts of propylene glycol. The intramuscular fatal doses were found to be about 14 Gm. per Kg. body weight for rats, and about 7 Gm. per Kg. for rabbits. The intravenous fatal doses were found to be about 16 Gm. per Kg. for rats, and about 5 Gm. per Kg. for rabbits. Practically no effects were observed in rats from drinking water containing less than 10% propylene glycol; but with higher concentrations the fluid intake was greatly restricted, and the animals lived only a few days. No definite microscopic changes were observed in organs of the animals sacrificed at the end of the experimental period of 140 days. It is interesting to note that these authors found the intravenous fatal dose for rats to be greater than the intramuscular fatal dose, a relationship rarely observed. This is particularly significant since the intravenous fatal dose for another rodent (rabbit) was found to be considerably less than the intramuscular fatal dose, which is the usual relationship.

Braun and Cartland (2) investigated the acute toxicity of propylene glycol for rats by subcutaneous, intramuscular and intravenous injections, and obtained results which were in satisfactory agreement with those reported by Seidenfeld and

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Hanzlik. In addition Braun and Cartland investigated the acute toxicities on oral administration to rabbits.

EXPERIMENTAL METHODS AND RESULTS.

Acute Toxicity.—In the acute experiments propylene glycol was administered intravenously to rabbits; and orally, subcutaneously, intramuscularly and intravenously to white rats. All animals were adults, but otherwise unselected as to age, source, weight or sex, and were maintained on standard diets (Purina). The animals given propylene glycol orally received no food for twenty-four hours prior to the experiment.

The results of the acute toxicity experiments are shown in Table I. The Average Fatal Dose is taken as the quantity required to kill 50% of the animals. This figure was arrived at by plotting dose against per cent mortality, and then deriving the fatal dose for 50% of the animals from the curve so constructed. In Table II is shown a summary of the data published by various authors to whom references are made. These figures also represent doses fatal to 50% of the animals, and were derived from data published by the original authors. In many instances the number of animals used for each dose was so small as to make the accuracy of such a procedure questionable. One author used only four mice in the entire series. However, since there is no consis-

TABLE I.—TOXICITY OF PROPYLENE GLYCOL.

Dose (per Kg. Body Wt.). Cc.	Gm.	Number Animals.	Died.	Lived.	% Mortality
		* Oral Administration: Rats.			
25	26.0	5	0	5	00
30	31.2	5	2	3	40
35	36.4	5	3	2	60
		Subcutaneous Administration: Rats.			
20	20.8	5	1	4	20
25	26.0	5	4	1	80
30	31.2	5	5	0	100
		Intramuscular Administration: Rats.			
12	12.48	5	0	5	00
14	14.56	5	3	2	60
16	16.64	5	4	1	80
18	18.72	5	5	0	100
		Intravenous Administration: Rats.			
6	6.24	10	1	9	10
7	7.28	5	4	1	80
8	8.32	10	8	2	80
9	9.36	5	5	0	100
10	10.40	5	4	1	80
12	12.48	5	5	0	100
		Intravenous Administration: Rabbits.			
5	5.2	3	0	3	00
6	6.24	5	1	4	20
7	7.28	5	4	1	80
8	8.32	5	5	0	100

* Larger doses were impractical due to limited capacity of rat's stomach.

TABLE II.

Animal.	Method of Administration.	Propylene, Gm./Kg.	Diethylene, Gm./Kg.	Ethylene, Gm./Kg.
Mouse	Subcutaneous	...	...	5.6 (3)
Rat	Oral	33.5 (6)	16.8 (4)	...
Rat	Subcutaneous	22 (2)	15.7 (4)	...
		22.5 (6)	...	...
Rat	Intramuscular	14 (1)	7.87 (4)	4.2 (5)
		15.5 (2)	...	...
		14 (6)	...	...
Rat	Intravenous	16 (1)	4.75 (4)	...
		18.9 (2)	...	...
		6.8 (6)	...	...
Rabbit	Oral	19.3 (2)	...	...
Rabbit	Intramuscular	7 (1)	3.9 (4)	6 (5)
Rabbit	Intravenous	5 (1)	2.25 (4)	4.7 (5)
		6.5 (6)	...	...

Numbers in parentheses refer to papers from which these data were obtained. The data represent Average Lethal Doses (50% mortality) calculated from data published by the various authors.

tency in the per cent mortality taken by various authors as indicating Average Fatal Dose, it is believed that this treatment of the data gives results which are more nearly comparable. The intravenous fatal dose for rabbits, and the intramuscular fatal dose for rats agree satisfactorily with those reported by Seidenfeld and Hanzlik, but the intravenous fatal dose for rats was found to be far less than that reported by these authors. Also, results obtained from subcutaneous and intramuscular injections in rats were in excellent agreement with those reported by Braun and Cartland, but again there was a marked discrepancy in the intravenous fatal doses for rats. When this discrepancy first became apparent it was thought that perhaps diet, age or some other uncontrolled factor may have been responsible, but the experiment has since been repeated on two different occasions on animals from other sources of supply. Essentially the same results were obtained on all three groups of rats, those from two groups being included in Table I.

During the early attempts at injections into veins of the tails of rats it was observed several times that the needle passed completely through the vein and into loose tissue surrounding the vein. Then, upon aspiration with the syringe, a droplet of blood was drawn into the syringe, giving a false indication of the position of the needle. This droplet of blood was the result of leakage from the punctured vein, and was not obtained directly from the lumen of the vein. Upon injecting the contents of the syringe the vein was obliterated by external pressure of the injected material on the vein. This material passed toward the body through tissues surrounding the vein, and ultimately most of it accumulated in muscular and subcutaneous tissues at the base of the tail. Such injections gave many of the appearances of intravenous injections without actually having been intravenous. It was found that such accidents could be obviated almost entirely by first placing the rat's tail in water at a temperature of about forty degrees Centigrade for one or two minutes before attempting the injection. This caused dilatation of the veins so that the needle could be introduced quite easily, and with little danger of failure.

Neither Seidenfeld and Hanzlik nor Braun and Cartland mentioned the veins selected by them for injections. Concerning these injections Braun and Cartland state: "The intravenous injection of undiluted propylene glycol produced rapid obliteration of the veins making administration very difficult. At doses of 16 to 19 cc. per Kg. intravenously, all rats showed marked muscular tremors and later became comatose." The authors of this communication did not find the administration of propylene glycol difficult after previous dilatation of the vein as mentioned above, nor were the veins rapidly obliterated. With sub-lethal doses, the veins were seen to refill with blood just about as promptly after withdrawal of the needle as if saline or glucose solutions had been injected. Following fatal doses death occurred within a short time in most instances, although with barely fatal doses the animals sometimes lived for ten or fifteen minutes; exceptionally one lived as long as several hours.

The data presented by Seidenfeld and Hanzlik in their Table I suggests that some such accident as previously described may have happened in many of their injections. An increase in dose from 9 cc. to 12 cc. per Kg. was accompanied by a drop in fatalities from 30% to 20%, and a further increase in dose to 15 cc. per Kg. was accompanied by an increase in fatalities to only 40%. To increase the number of fatalities from 30% to 70% it was found necessary to increase the dose from 9 cc. to 18 cc. per Kg. One would predict just such a relationship between dose and number of fatalities if approximately 30% to 40% of the injections actually were made into veins. Then, upon approaching the intramuscular fatal dose (variously reported between 14 and 15.5 Gm. per Kg.) the mortality rate would naturally approach that for the intramuscular method of administration. The fact that the intravenous fatal dose was found by Seidenfeld and Hanzlik actually to exceed the intramuscular fatal dose may have been due to retention of part of the injected material in the tissues of the tail, from which absorption was exceedingly slow because of obliteration of the vein.

Symptoms following the administration of fatal or near fatal doses of propylene glycol were found to be essentially as described by Seidenfeld and Hanzlik and Braun and Cartland. The fatal period varied from a minimum of two or three minutes following intravenous injections to a

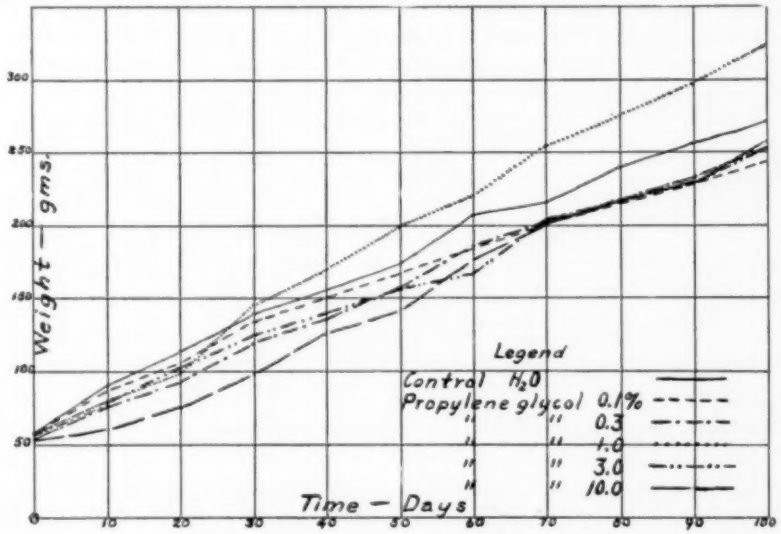

Fig. 1.—The effect on the growth of white rats of adding various concentrations of propylene glycol to the drinking water.

maximum of about two days following oral administrations. Muscular tremors and mild clonic convulsions occurred frequently. The animals became comatose more or less rapidly depending on the method of administration. Hematuria was observed frequently, especially after intravenous injections.

Chronic Toxicity.—The chronic toxicity of propylene glycol was investigated by administering the substance to growing rats by way of their drinking water. Male rats at weaning age (about 55 Gm. average weight) were used in groups of five animals each. Propylene glycol was added to the drinking water in concentrations of 0.1%, 0.3%, 1.0%, 3.0% and 10.0% by weight. A control group received distilled water instead of propylene glycol solution. All animals received the diet recommended by Osborn and Mendel. Food and drink were allowed ad libitum. Weights of the animals and consumption of food and drink were recorded at five-day intervals for the duration of the experiment—100 days. At the end of this period all surviving animals were sacrificed, and all internal organs were prepared for microscopic examination. During the first ten days of the experimental period those animals which received 10.0% propylene glycol increased in weight less rapidly than the remainder of the animals, and appeared to be in poor physical condition. However, very soon thereafter, those animals recovered from their poor start, and began to increase in weight at a rate about equal to that of the control group. Two animals which received

10.0% propylene glycol and one which received 1.0% died before the termination of the experiment. Growth curves for the six groups of animals are shown in Fig. 1. No significant differences were noted in consumption of food and drink by the various groups. It is worthy of note that those animals which received 10.0% propylene glycol solution consumed from 9.6 to 15.8 Gm. per Kg. per day, whereas, the acute oral fatal dose was found to be 33.5 Gm. per Kg.

Microscopic examination of organs from these animals was made by Doctor G. Z. Williams, Associate Professor of Pathology of this institution. In no way were the organs from animals which had received propylene glycol found to differ from those of the control group, which had received distilled water. These results substantiate those reported by Seidenfeld and Hanzlik from a similar experiment.

Hemolysis.—The frequent occurrence of hematuria following administration of sub-lethal doses of propylene glycol to rats, and the previous mention of this action by Von Oettingen and Jirouch (3), prompted a study of this phenomenon *in vitro*. Isotonic solutions of diethylene glycol and propylene glycol were prepared (0.278 molar). These solutions were mixed with varying quantities of 0.9% NaCl solution so that a series of mixtures resulted which contained isotonic glycol and isotonic saline in the proportions of 9 to 1, 8 to 2, 7 to 3, 6 to 4, and so on. A separate series of solutions was prepared by diluting isotonic saline with distilled water in the same manner. These last solutions were used for ascertaining the fragility of the red corpuscles, and whether or not the blood used was normal in this respect. One drop of human blood was added to each tube, which contained 5 cc. of one of the solutions prepared as described above. The results are shown in Table III. Three such experiments were performed, each with blood from a different individual.

TABLE III.—HEMOLYSIS FROM DIETHYLENE GLYCOL AND PROPYLENE GLYCOL.

Tube No.	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.
Dilution	0	9/10	8/10	7/10	6/10	5/10	4/10	3/10	2/10	1/10
Molar conc.	0.278	0.250	0.222	0.195	0.167	0.139	0.111	0.083	0.056	0.028
Diethylene	xxxx	xxxx	xxxx	xxxx	xxxx	x	0	0	0	0
Propylene	xxxx	xxxx	xxxx	xxxx	xxxx	x	0	0	0	0
Saline	0	0	0	0	0	x	0	0	0	0
Conc. saline	0,9%	0.81%	0.72%	0.63%	0.54%	0.45%	0.36%	0.27%	0.18%	0.09%

xxxx indicates complete hemolysis. 0 indicates no hemolysis.

Fragility of corpuscles was normal in each instance, and there was no significant variation in the effects of the glycols. The line of demarcation between hemolysis and non-hemolysis was very definite. Methemoglobin could not be detected in any of the tubes by means of a small hand-spectroscope.

NOTE: Since the above experiments were completed, Lehman and Newman (7) reported results from somewhat similar experiments. These authors found that if propylene glycol solutions were prepared with a final concentration of 0.9% NaCl, then no hemolysis occurred with glycol concentrations of 30% or less; but that if distilled water were used as a diluent, hemolysis occurred in all dilutions. Thus, 0.9% NaCl seems to have afforded marked protection against hemolysis. The explanation for this apparent protection probably lies in the fact that certain substances penetrate the red cell membrane so rapidly that they exert no appreciable osmotic effect on the cell. Therefore, aqueous solutions of propylene glycol behave essentially as distilled water, and produce rapid and complete hemolysis; whereas, the presence of 0.9% NaCl provides an approximately isotonic medium in the presence of less than 30% glycol. This explanation was offered for the same type of phenomenon observed by Johnson, Carlson and Johnson (8) in connection with the hemolytic action of glycerine. These latter authors also stated that a similar situation exists with respect to aqueous solutions of urea. On the basis of data presented in Table III, it appears that dilution of 0.9% NaCl solution with 0.278 molar solutions of either propylene or diethylene glycol was equivalent to dilution with distilled water in so far as production of hemolysis was concerned. These results are therefore in accord with the observations of Lehman and Newman and Johnson, Carlson and Johnson.

SUMMARY.

1. In rats the acute Average Fatal Dose of propylene glycol was found to be 33.5 Gm. per Kg. orally, 22.5 Gm. subcutaneously, 14 Gm. intramuscularly and 6.8 Gm. intravenously. These figures are in agreement with those reported by other authors, with the exception of the intravenous fatal dose, which is somewhat less than half that reported by other authors. Reasons are given for believing the lower figure to be correct for the intravenous fatal dose.

2. In rabbits the acute Average Fatal Dose on intravenous administration was found to be 6.5 Gm. per Kg.

3. The chronic toxicity of propylene glycol was studied by the administration of the material to growing rats by way of their drinking water. Concentrations of 3% or less caused no appreciable change in rate of growth. A concentration of 10% caused a temporary slowing in rate of growth which lasted for about ten days. Rate of growth after this initial slowing became essentially normal. No significant changes were found on microscopic examination of organs of these animals sacrificed at the end of the experimental period of 100 days.

4. Hematuria was observed following the intravenous administration of sublethal doses of propylene glycol to rats. Hemolysis was produced *in vitro* by both diethylene glycol and propylene glycol in concentrations greater than 0.14 molar. This *in-vitro* action seems to be due to the dilution of isosmotic NaCl solution with the osmotically inactive glycol solution, rather than to a specific hemolytic action of these glycols in the dilutions used.

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LIQUOR ANTISEPTICUS.*

BY H. S. HOWELL,[1] LOUIS GOLDBERG,[1] R. K. SNYDER[1] AND E. N. GATHERCOAL.[1]

BORIC ACID IN LIQUOR ANTISEPTICUS.

The following statement in the N. F. VI monograph on Liquor Antisepticus has been criticized on the basis that the limits on these residues were not always attainable:

"Evaporate 10 cc. of the solution at 100° C.: not more than 0.184 Gm. of a white crystalline residue remains. Add 10 cc. of alcohol to this residue and ignite: the flame is enveloped with a green mantle and not less than 0.042 Gm. of residue remains."

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* National Formulary Research Project F7 at the University of Illinois College of Pharmacy. This is but an abstract of the original paper which is given in full in the National Formulary Bulletin, pages 2682–2689.

[1] National Formulary Laboratory.

Residue values were obtained by this test on nine lots of N. F. antiseptic solution prepared in the laboratory or obtained commercially. While the values in each case meet the official standards, yet the varying results, even on the same solution, are unsatisfactory. These variations are probably due to the effect of heat on boron compounds.

The following assay for boric acid has been developed in this laboratory.

Dilute Tumeric T.S. to fifteen times its volume with alcohol. Dissolve 2.5 Gm. (this could be made 2.4, 2.3 or even 2.2 Gm.) of boric acid, in a sufficient quantity of a 30 per cent alcohol-water mixture to make exactly 100 cc. of a boric acid standard solution. Mix 2.0 cc. of the tumeric dilution with 25 cc. of antiseptic solution, and another 2.0 cc. of the tumeric dilution with 25 cc. of the boric acid standard solution. Allow the mixtures to stand for ten minutes and then compare them in a colorimeter. The intensity of color developed in the mixture containing the antiseptic solution is not less than that developed in the mixture containing the boric acid standard solution.

NOTES.

(1) The color developed by the boric acid and tumeric is distinctive and considered to be a confirmative test for either item, and is frequently used as such.

(2) The test has shown that it is accurate to at least 96 per cent of the theoretical content of boric acid.

(3) The test is more accurate and more indicative of boric acid than the residue test now in the monograph. There is no interference from the other compounds in the antiseptic solution.

INCOMPATIBILITY OF THYMOL AND CHLORTHYMOL WITH EUCALYPTOL.

When the N. F. V monograph of Liquor Antisepticus was revised, 1.0 Gm. of chlorthymol was added to increase the antiseptic power of the solution. At the same time the amount of eucalyptol was reduced from 5 cc. to 2 cc. The N. F. VI formula has been criticized on the basis that chlorthymol is incompatible with eucalyptol.

Assay of Thymol and Chlorthymol.—An attempt to estimate thymol and chlorthymol in alcoholic solutions and in aqueous-alcoholic solutions, both in the absence of and the presence of eucalyptol, has been made by adapting the method tentatively adopted by the Association of Official Agricultural Chemists and developed by Leslie Hart, Associate Referee, U. S. Food and Drug Administration, St. Louis, Mo., to our purposes. Each cc. of tenth-normal bromine is equivalent to 0.003753 Gm. of thymol, 0.009228 Gm. of chlorthymol or 0.002667 Gm. of each in equal parts by weight.

1. The determination of the thymol or chlorthymol in simple alcoholic solutions by direct titration with tenth-normal bromine gave 100% results. In each of the other determinations the assay process was used and this gives consistently lower results, from 92.4% to 99.5%, mostly 96% and 97%.

2. Solutions in alcohol or in alcohol 1 vol.—water 3 vols., of thymol, of chlorthymol, or of thymol and chlorthymol are clear without filtration. When eucalyptol is added to these alcoholic solutions they still remain clear, but when water is then added, the clear solutions become very cloudy. It is evident that incompatibility, due to the eucalyptol, occurs when thymol or chlorthymol with eucalyptol is dissolved (?) in a mixture of alcohol 1 vol.—water 3 vols.

3. When the cloudy mixtures of No. 2 are well shaken and assayed, nearly 100% of the thymol or chlorthymol or both is determined.

4. When the cloudy mixtures of No. 2 are filtered until clear, the assay shows a loss of about one-third of the thymol and two-thirds of the chlorthymol. Probably the incompatibility is of a physical nature rather than chemical.

5. Liquor Antisepticus, *i. e.*, the product after filtration, has lost much of the thymol and chlorthymol used in its preparation.

6. L. Hart, who developed this assay method, obtained results varying from 90% to 103% of theory, while in this laboratory results vary from 82.2% to 99.8% of theory. The variation in results possibly lies in the difficulty in obtaining proper extraction with the solvents.

NEW FORMULA PROPOSED FOR LIQUOR ANTISEPTICUS.

From the experiments previously recorded it is evident that in the present official formula the flavoring ingredients cause precipitation of a considerable proportion of some of the active ingredients.

All of the ingredients in the present official formula are soluble, individually, in the solvent except eucalyptol. Experiments indicated that 0.8 cc. of eucalyptol was the maximum quantity that could be dissolved in a solvent composed of alcohol 300 cc. and water *q. s.* 1000 cc. When 1.0 Gm. of chlorthymol was introduced into this solution, immediately an oily globule formed on the surface and upon shaking the mixture became turbid.

Eucalyptol 0.1 to 0.2 cc. was the maximum amount that could be dissolved in a solution of 1.0 Gm. of chlorthymol in a mixture of alcohol 300 cc. and water *q. s.* 1000 cc.

When to the clear solution mentioned in the previous paragraph, 1.0 Gm. of menthol was added, an oily globule formed on the surface. These globules were tested for "chloride" by the Volhard method, but poor results were obtained.

If all of the thymol and chlorthymol be retained in the finished solution, the present official quantities could be reduced by one-half and the antiseptic power remain greater than at present.

Methyl salicylate does not affect precipitation; neither does menthol when reduced to 0.5 Gm. in the formula. The oil of thyme, however, requires careful adjustment, yet is important in developing the flavor.

After many combinations were tried, the following formula seemed to be most satisfactory:

Boric acid	25.0 Gm.
Thymol	0.5 Gm.
Chlorthymol	0.5 Gm.
Menthol	0.5 Gm.
Methyl salicylate	0.2 cc.
Eucalyptol	0.1 cc.
Oil of thyme	0.01 cc.
Alcohol	300.0 cc.
Water, a sufficient quantity,	
To make	1000.0 cc.

Dissolve the boric acid in 650 cc. of hot water and allow the solution to cool. Dissolve the other ingredients in 300 cc. of alcohol. Mix the two solutions and

add sufficient water to make 1000 cc. Allow to stand in a tightly closed container for 24 hours and filter.

This solution when first mixed is perfectly clear if a reagent grade of boric acid is used. Commercial U. S. P. boric acid frequently causes a slight cloudiness. However, upon standing for a day or so, a slight cloudiness always develops. Apparently this trace of turbidity has no effect on the thymol and chlorthymol, as assays on the filtered and unfiltered solutions show identical results. The aroma and taste of the new antiseptic solution differ slightly from the present official solution and the acridity and pungency is notably less. It is the concensus of opinion in this laboratory that the odor and taste are more pleasant than those of the official article.

The antiseptic power of the proposed preparation is higher than that of the official preparation. It kills the test organism, under the conditions of the test, in one minute instead of five minutes as allowed by the test. Even in half strength it will kill the test organism in one minute.

SUMMARY.

1. The limits on the residues from the boric acid obtained by the evaporation and the ignition tests of N. F. VI are not fully satisfactory.

2. An adaptation of the tumeric test for boric acid serves for the qualitative and quantitative determination of boric acid in Liquor Antisepticus.

3. An incompatibility that occurs during the preparation of Liquor Antisepticus is apparently physical in nature and occurs when eucalyptol above 0.02 per cent is added to the aqueous-alcoholic solution of thymol or chlorthymol or both.

4. The A. O. A. C. tentative assay for thymol has been used on solutions of thymol, and adapted to solutions of chlorthymol and Liquor Antisepticus.

5. A formula for Liquor Antisepticus which is unchanged from the official formula, except in the proportion of certain of the ingredients, is offered. It presents no incompatibilities, is more highly antiseptic than the present official solution, is not so acrid or pungent in taste, yet preserves the same aroma, is less difficult to compound and is less expensive.

A STUDY OF DATURA STRAMONIUM.*

BY FRANK H. EBY,[1] FREDERICK M. SCHOLL[2] AND DAVID J. PHILLIPS.[3]

Datura Stramonium Linné is one of the two well-known species of Datura found in Pennsylvania. Within the limits of the city of Philadelphia it frequently thrives in impoverished soil and even where conditions are most unfavorable for the development of many uncultivated plants, Stramonium frequently grows to a height of two meters, produces large stems and rank foliage and otherwise exhibits most of the normal vegetative characteristics.

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Studies showing the effects of soil composition, fertilizers and methods of collection have been reported in recent years. Maurin (1) reported that variation in soil composition produced a variation in the growth of plants and the production of alkaloids.

This paper contains a report of a study conducted to determine (1) if an extremely poor environment produced a marked decrease in the alkaloidal content of Datura Stramonium and (2) the distribution of the alkaloids in the plant.

All material used in the study was collected from uncultivated plants which grew within the city of Philadelphia in vacant lots where Stramonium had been established for a number of years. In every instance the plants grew in soil which was unusually poor since it consisted largely of debris from demolished buildings. The plants attained an average height of 1.5 meters, produced rank foliage and an abundance of fruits and seeds. For several years previous to 1935, when the first material was collected, the areas which supplied the material for this study were carefully observed and at no time was there any indication of retarded plant growth due to the poor environment.

All plant parts used in the study except fruits and seeds were collected in the early part of September of 1935 and 1936. Parts were carefully separated at the time of collection and rapidly dried in well-ventilated trays. Fruits and seeds were collected in October, before frost, when the fruits began to dehisce. All specimens were reduced to a fine powder and preserved in air-tight containers until they were extracted.

EXPERIMENTAL.

Ten grams of each specimen, in fine powder, were extracted by percolation and assayed by the process prescribed in the U. S. P. XI.

TABLE I.—RESULTS.

Plant Part or Parts.	Season Collected.	Sample.	Per Cent Total Alkaloids.
Leaves and flowering tops	1935	1	0.237
	1935	2	0.312
	1935	3	0.310
	1935	4	0.444
Leaf blades and petioles	1935	1	0.278
	1935	2	0.301
	1935	3	0.301
	1935	4	0.295
	1935	5	0.303
	1935	6	0.462
Leaf blades more than 25 mm. in length	1935	1	0.165
	1935	2	0.281
	1935	3	0.239
	1935	4	0.237
	1936	5	0.160
	1936	6	0.160
	1936	7	0.156
	1936	8	0.144
	1936	9	0.164
	1936	10	0.144
	1936	11	0.151
	1936	12	0.191
	1936	13	0.160

TABLE I.—(*Continued from page 473.*)

Leaf blades less than 25 mm. in length	1935	1	0.420
	1936	2	0.391
	1936	3	0.290
	1936	4	0.340
Petioles from large leaves	1936	1	0.359
	1936	2	0.791
	1936	3	0.551
	1936	4	0.705
	1936	5	0.791
	1936	6	0.803
Stems less than 8 mm. in diameter	1935	1	0.110
	1935	2	0.093
Stems more than 8 mm. in diameter	1935	1	0.029
	1935	2	0.109
	1935	3	0.104
	1935	4	0.127
	1935	5	0.144
	1936	6	0.179
	1936	7	0.145
	1936	8	0.202
Flowers	1936	1	1.040
Fruits not including seeds	1935	1	0.101
	1935	2	0.080
	1935	3	0.120
	1936	4	0.060
	1936	5	0.075
Seeds	1935	1	0.422
	1935	2	0.416
	1935	3	0.537
	1935	4	0.376
	1935	5	0.393
	1935	6	0.434
	1935	7	0.514
	1935	8	0.451
	1935	9	0.434
	1935	10	0.434

CONCLUSION.

Environment considered entirely unsatisfactory for the normal development of most plants did not appear to retard the growth of Stramonium and the production of alkaloids was not materially affected.

REFERENCE.

(1) Maurin, *Bull. sci. pharmacol.*, 32, 75 (1925).

A CHLORAL DERIVATIVE OF LEVULINIC ACID.

BY HAROLD W. COLES.*

INTRODUCTION.

While searching for a substitute for chloral as a hypnotic, Hanriot and Richet (1) at first studied the chloralides and, in particular, the lactic chloralide. Contrary to their anticipations, however, the lactic chloralide did not have any hypnotic powers and caused serious organic troubles in the animals. The chloraloses were then investigated, and alpha-chloralose gave excellent results (2).

The sleep produced by the chloralose does not resemble that produced by chloral, for the reflexes are neither abolished nor diminished, and indeed are increased. It is a substance much more active than chloral, and six hundred mg. per Kg. body weight does not cause death in the dog. Yet, while chloralose is a considerable step ahead itself in being more active and less toxic, and while it compares favorably (3) with other hypnotics, it is still lacking in several respects.

The alpha-chloralose, although much more soluble than the beta-isomer, is still only slightly soluble in water and has a disagreeable bitter taste. It is often unreliable in its effects. Frequently no hypnosis occurs under fatal doses, and some observers have reported transitory by-effects as trembling, spasms, epileptoid or cataleptoid attacks, dizziness, hallucinations and delirium.

Probably some of the uncertainty of the chloralose action is due to the fact that it still retains unchanged its aldehyde group.[1] It occurred to the author that chloral joined to a substance with an acid group might combine both stability and solubility since a sodium salt could be made. Levulinic acid suggested itself as the proper compound to join to the chloral since it offered a promise of being available commercially and inexpensively (4). Furthermore, the chloral-levulinic acid permits the pharmacological study of a different type of chloral linkage, being joined to the levulinic acid, carbon to carbon, through a double bond, while in the chloralides (chloraloses) the chloral is attached through oxygen (5).

The chloral-levulinic acid was prepared and also a number of its derivatives for identification purposes. The chloral-levulinic acid, although the chloral portion made up fifty-three per cent of the entire molecule, had no hypnotic activity. This surprising result will be discussed later in this paper.

The chloral derivative of levulinic acid should not be confused with the levulochloraloses already described (6) as those compounds are chloral derivatives of levulose, the sugar.

EXPERIMENTAL.

Condensation of Chloral with Levulinic Acid.[2]—A number of different condensing agents were tried before a suitable one was found. Gaseous hydrochloric acid (7) resulted in a very small yield and the product was difficult to obtain in a pure condition. The use of anhydrous calcium sulfate (Drierite) (8) in a sealed tube with a few drops of sulfuric acid gave a nicely crystalline compound which, on analysis, revealed a much too high percentage of chlorine.

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* Senior Industrial Fellow, E. R. Squibb & Sons Industrial Fellowship, Mellon Institute.

[1] It reduces Fehling's solution on boiling and forms a hydrazine, although in Meyer-Jacobson, Vol. 1, page 930, the general statement is made that the chloraloses do not reduce Fehling's solution.

[2] Courtesy of Dr. G. J. Cox, Mellon Institute.

The reaction was carried out at 115–120° for 5 hours. Long needles, melting at 135° (U. S. P. corr.), giving a smoky luminous flame, and a Beilstein test for halogen were obtained. The crystals are soluble in all alcohols, chloroform, ether, benzene, xylene, acetone, amyl acetate, petroleum benzin; insoluble in hot and cold water, sodium bicarbonate; difficultly soluble in hot sodium hydroxide. No red color was produced with concentrated sulfuric acid (9). Analysis: C, 26.57%; H, 2.20%; Cl, 53.29%. Calculated for monochloral-levulinic acid: C, 34%; H, 3.2; Cl, 43.34%. The compound gave a phenylhydrazine derivative containing 4.15% nitrogen (micro-Dumas). Calculated percentage nitrogen for a derivative of monochloral-levulinic acid is 8.34%. It is believed to be a dimol derivative.

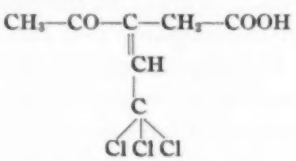
Esters of levulinic acid can be prepared in excellent yields with Drierite present to remove the water as rapidly as it is formed. This esterification was not exhaustively studied for optimum yields.

It was found that freshly fused sodium acetate was the best condensing agent (9). One mole equivalent of pure levulinic acid, one mole equivalent of freshly distilled chloral and one mole equivalent of freshly fused sodium acetate were mixed together and placed on a water-bath under a reflux condenser. The mixture became cloudy, darkened in color and became quite viscous. After four hours it was allowed to cool, then poured into distilled water. The supernatant liquid was decanted from the black syrup and the syrup washed repeatedly with distilled water. The dark syrup was then dissolved in about ten volumes of absolute alcohol, decolorized as much as possible with Norite, and the alcoholic filtrate reduced to a small volume. On standing, long needles separated out which were filtered off, washed repeatedly with a cold alcohol-water mixture (1:1) and dried at 80°. These crystals (best yield—30 per cent) have a melting point[1] of 113.5° C. and analyzed as follows:

Calculated for $C_7H_7O_3Cl_3$: Cl, 43.34%
Found:[2] (Parr Bomb method) Cl, 43.32%.

The crystals are quite insoluble in water, but are readily soluble in most organic solvents, glacial acetic acid and aqueous alkaline solutions. Cold dilute potassium permanganate is rapidly decolorized. Rapid decomposition takes place on vacuum distillation. The dry sodium salt tends to absorb moisture, and dissolves readily in water to give a neutral reaction. The chloral-levulinic acid does not produce the intense red color in concentrated sulfuric acid reported by Erdmann (9) for the benzylidene levulinic acid.

The compound is assigned the structure



on the basis of the literature records for analogous compounds (7, 9, 10). The proof advanced by earlier workers for beta-condensation under these conditions is questioned, and is being studied in connection with another problem.

The beta-chloral-levulinic acid gave a Beilstein test for halogen.[3] A compound of unknown structure was isolated from the condensation side-products, separating out of a glacial acid solution of impure chloral-levulinic acid.[4]

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[1] All melting points are corrected for stem exposure.

[2] Analyses by Mr. Saul Gottlieb, Columbia University.

[3] Levulinic acid, highly purified, also gave a Beilstein test for halogen, although there was insufficient halogen present to produce even a cloudiness with silver nitrate. Levulinic acid and its ethyl ester decolorize potassium permanganate in alkaline and neutral solution.

[4] Long, white needles, melting at 155.5–156°. Analysis revealed C, 26.70%, H, 2.17% and Cl, 54.30%. It is probably a compound containing two chloral residues. Calculated for one such substance ($C_9H_8O_4Cl_6$): C, 27.5%; H, 2.05%; Cl, 54.16%.

Bromination of Beta-Chloral-Levulinic Acid.—A satisfactory crystalline dibromide derivative has not yet been obtained. When finely powdered beta-chloral-levulinic acid is exposed to bromine vapor in a desiccator, fifty per cent excess bromine over that required for formation of a dibromide is absorbed, and the crystalline material becomes liquid. On exposure to the air, most of the excess bromine is given off, but no crystalline material could be isolated.

Derivatives of Beta-Chloral-Levulinic Acid.—These derivatives, the physical characteristics of which are given in the table, were prepared by the usual methods with the exception of the oxime where the suggestion of Bryant and Smith (11) as to the use of pyridine was followed.

TABLE OF DERIVATIVES.

Derivative.	Color.	M. P.	Nitrogen Per Cent (Micro-Dumas). Calculated.	Found.
p-Nitrophenylhydrazone	White	182°	11.03	11.29
Semicarbazone[1,2]	White	205.5–206°	13.88	13.63
p-Bromophenylhydrazone	White	161°	6.74	6.59
β-Naphthylhydrazone	Pinkish	188–189°	7.27	7.50
Phenylhydrazone	White	174.5°	8.35	8.12
Oxime[1,2]	White	103–104°	5.37	5.35
Thio-semicarbazone	White	177–177.5°	13.19	13.01

[1] Soluble in all alcohols, ketones, dioxan, chloroform, amyl acetate, benzene, dibutyl phthalate, hot water; insoluble in pentene-2, petroleum benzin.

[2] Soluble in concentrated sulfuric acid without color production.

DISCUSSION.

Beta-chloral-levulinic acid administered orally to rats, either as the free acid or soluble sodium salt, did not show any hypnotic activity in doses of 1500 mg. per Kg. weight of animal.[1] No toxic effect was noticed. This surprising lack of activity is probably due to the stability of the substance (no chloroform is produced on boiling with alkaline solutions) and to the inability of the rat to hydrolyze off the chloral residue. It is not believed likely that the condensation of the chloral group with levulinic acid in the alpha- or gamma-position would result in a compound any more satisfactory, as these types of derivatives are likewise stable.

SUMMARY.

1. A new derivative of levulinic acid, namely, chloral-levulinic acid, has been prepared.

2. Chloral-levulinic acid, in relatively large quantities, is non-toxic and non-hypnotic when given orally to rats.

3. Seven nitrogen derivatives of chloral-levulinic acid are described for purposes of identification.

The author wishes to thank Dr. George D. Beal, Assistant Director of Mellon Institute, for his advice during the progress of this work.

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[1] The author is indebted to Mr. H. A. Holaday and associates of the E. R. Squibb & Sons Biological Laboratories, New Brunswick, N. J., for these tests.

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(7) Sen and Roy, *J. Indian Chem. Soc.*, 7, 404 (1930).

(8) Hammond, St. Petersburg Amer. Chem. Soc. Meeting (March 1934).

(9) Erdmann, *Ber.*, 18, 3441 (1885).

(10) Borsche, *Ibid.*, 47, 1108 (1914); 48, 842 (1915); Kehrer and Kleberg, *Ibid.*, 26, 345 (1893); Erdmann, *Ibid.*, 21, 635 (1888); 24, 3201 (1891); Ludwig and Kehrer, *Ibid.*, 24, 2776 (1891); Erlenmeyer, *Ibid.*, 23, 74 (1890); Erdmann, *Ann.*, 254, 182, 197, 218 (1889); 258, 129 (1900).

(11) Bryant and Smith, *J. Am. Chem. Soc.*, 57, 57 (1935). See also Bachmann and Boatner, *Ibid.*, 58, 2097 (1936); Gulati and Ray, *Current Science*, 5, 75 (1936); Cook, Hewett and Lawrence, *J. Chem. Soc.* (London), 71 (1936).

THE PRESENT STATUS OF ACONITE RESEARCH.*

BY WM. J. BONISTEEL.[1]

The fundamental problem in aconite research is to find an aconite or aconites that can be depended upon to yield a definite alkaloidal entity. This short paper is intended as a progress report and to show the pressing need for some important problems to be solved. In the Index Kewensis approximately 524 species of aconites are listed. How many of these types are correctly named remains to be seen. The mere publication of the species in the Kew Index does not indicate that such a species of plant is valid, although it may be an aconite type. Our U. S. P. definitions should be more precise. Over thirty types of napellus have been investigated and all would fit into the category of this genus, but preliminary tests show that much variation is present both from the morphological and chemical standpoint. From amorphous aconitine a colleague of mine has isolated a type of ephedrine alkaloid. Other breakdown products are now being investigated by this worker. Such research throws new light upon the structure of the aconitine molecule and the need for basic research in this group. Microchemical tests which will show the type of chemical present without growing huge amounts of the plant are greatly needed.

The problem of knowing just what you have with such a heterogeneous group of plants remains unanswered at present. The taxonomist merely gives his opinion. All the strains of aconites that yield aconitine should be grown. This work is now being carried on and there are over a hundred types in cultivation. Twice this number was once under cultivation but the inability to secure funds for this research resulted in a great loss. Each desirable strain is then propagated clonally by means of daughter tubers. The conception of the clone seems to have been overlooked in pharmaceutical investigations of drug plants. In this way a series of plants are grown until enough have been obtained to give material sufficient for an adequate chemical investigation. A hundred pounds of dried root material would give ap-aproximately a half pound of crude alkaloid for both chemical and pharmacological investigation. It would take about 1000 plants for this work. Naturally such a problem is slow work, takes much land and many hands to cultivate, and much bookkeeping for records. By this method we are certain of the source of the plant. Its chemical characters will not fluctuate. We have established a unit for future

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* Presented before the Scientific Section, A. PH. A., New York meeting, 1937.

[1] Professor, Fordham University.

work. Unfortunately much of our chemical work is nullified by the inability of the chemist to be absolutely certain of his crude material. Somewhere a drug garden should be established for the continued growth of such plants for future research workers. We hope to breed plants for both high and low toxicity. Much valuable work has been done on the standardization but its value would have been enhanced if they had known the source, parentage and type of plant with which they were dealing. When sufficient plants have been grown for the purpose outlined the writer hopes to have others in the field of chemistry and pharmacology assist in the tabulation of results.

In the plant breeding work we have been forced to develop new methods of cultivation and have made several trips to regions where aconites grow naturally. The flower behavior of the plant needed to be restudied. The dichogamy has been studied and now awaits publication. Seed germination has been studied and in certain groups we can get germination in seven days by means of chemical treatment but in others much work remains to be accomplished. Fresh seeds are hard to get and from many lots not a single plant can be obtained. From a horticultural standpoint the details have already been published in "House and Garden."

The cytology of the aconites must be well known in order that time may be conserved in the breeding work. Chromosome counts have been made by Langlet, Affify, Schafer, LaCour and myself. The basic number is 8. The section *Lycoctonum* appears diploid and the section *Anthora* is tetraploid. The section *Eu-Aconitum* contains diploids, triploids, tetraploids, hexaploid and octoploid forms. Thus the chromosome range runs from 16 to 64. So far no aconite has been found with a chromosome number of 40 or 56. When we have sufficient plants growing for chemical analysis we want to correlate this with the chromosome number. It is in this category that many interesting problems lie. With several interspecific hybrids the problem becomes fascinating, to say the least. The chromosome number has been determined for some of the native aconites and will be published in the near future.

Many of our hybrids are sterile. For the purpose of getting a definite aconite for alkaloidal purposes this field of endeavor seems to hold the most promise. With the ability to produce seeds lost through chromosome complexes we can thus keep such a valuable strain free from contamination with other plants. A few of these types are under cultivation at the present time and each year additional sterile plants are found in our hybrid population. The cytology of one hybrid type has been carried on for some time and we are just getting this material in shape for publication. Dr. A. B. Stout, of the New York Botanical Garden, has developed several seedless grapes that will grow in the region of central New York. No reason why we should not have several seedless plants growing for drug purposes. The pharmacognosist must be depended upon to be able to produce plants with known ancestry so that chemical work will have a better basic foundation for future investigations. Both fields should be more closely correlated in the future. It is a sheer waste of effort for the chemist to spend much valuable time on a problem and then find that he cannot again obtain the same material for his own or for other investigators.

Important problems yet to be solved are the chromosome numbers of other aconites not as yet determined. Much is yet to be done in the problem dealing with

sterilities. Sterilities concern not only aconites or drug plants but have an increasing bearing when dealing with human beings. It is from the plant that the fundamental concepts of this problem can best be procured. There are now plant collectors searching for new aconites, one part in the region north of India. Much more material is needed from the Far East and throughout all Asia, which seems to be the central point of dispersion for the aconites. Even all the aconites of our own country have not as yet been examined. Seed germination should be studied in more detail. Hybridizing these additional plants must be carried out and careful selection made for the best types. Plenty of time and money are needed in this type of research. When such projects are carried to the point that adequate material is available for our chemist, then and then only can we tell whether aconite deserves to be considered a useful drug plant or not. All drug plants should be treated in the same manner.

NOTE: Lantern slide plates used in the lecture will not be submitted for publication on account of the expense involved.

STABILITY OF IPECAC PREPARATIONS.*

BY SAMUEL W. GOLDSTEIN.

Very little work has been reported on the stability of ipecac preparations and the published results vary greatly. Roberts (1) observed that Wine of Ipecac deposited a sediment in which he found no trace of alkaloids upon examination after six months. Procter (2) stated that a Fluidextract of Ipecac prepared in 1859 with 87.5 per cent alcohol was in "perfect condition" after being undisturbed for four years. LaWall (3) found 2.76 per cent of alkaloid calculated as emetine in the clear supernatant liquid of a fluidextract prepared thirty-three years earlier and kept in a carefully sealed bottle. Wulling (4) reported that Acetic Extracts of Ipecac prepared with 6, 10 and 20 per cent acetic acid developed precipitates; while 50 per cent acetic acid yielded a product that remained clear. Guyer (5) reported that samples of Liquid Extract of Ipecac, B. P., which contained 2.0 per cent of alkaloids when prepared yielded 1.5 per cent of alkaloids after standing for two months. Thomson (6) found that samples of Liquid Extract of Ipecac, B. P. showed no loss in alkaloidal content after seven months.

In an earlier paper (7) the author reported on a series of extractions of ipecac using U. S. P. X and U. S. P. XI menstrua and acetic acid (9%). Part of the first percolates, which contained 61–85 per cent of the alkaloids extracted, were set aside in partly filled bottles standing in diffused sunlight. The behavior of these percolates on standing is reported herein.

EXPERIMENTAL.

The acetic acid extracts, on standing, became unsightly because of the continued sedimentation although they were filtered after three months and eight months. The preparations obtained using U. S. P. X and U. S. P. XI menstrua deposited small amounts of sediment and remained practically clear when filtered after standing for two months.

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* From the Laboratory of the Bureau of Chemistry of the Maryland State Department of Health.

The preparations were filtered at the intervals indicated and the filtrates were assayed for ether-soluble alkaloids (U. S. P. XI assay) and total solids (heated to constant weight in an oven at 100° C.). The results are given as per cent w/v in Tables I and II.

TABLE I.—RESULTS OF ALKALOIDAL DETERMINATIONS IN PER CENT W/V.

Menstrua.	Color of Bottle.	When Prepared.	After 3 Months.	After 8 Months.	After 16 Months.
U. S. P. XI	Blue	1.11	1.10	1.10	1.10
	Blue	1.07	1.09	1.03	1.02
U. S. P. X	Blue	0.83	0.82	0.82	0.82
Acetic acid (9%)	Blue	1.07	1.04	0.94	0.91
	Amber	1.20	1.18	1.14	1.14
	Flint	0.96	0.91	0.90	0.88
Large scale	Flint	1.21	....	....	1.18

TABLE II.—RESULTS OF TOTAL SOLIDS DETERMINATIONS IN PER CENT W/V.

Menstrua.	Color of Bottle.	When Prepared.	After 3 Months.	After 8 Months.	After 16 Months.
U. S. P. XI	Blue	15.47	14.92	14.95	14.96
	Blue	14.85	14.32	12.52	12.54
U. S. P. X	Blue	12.33	11.70	11.70	11.69
Acetic acid (9%)	Blue	19.58	19.24	15.92	14.94
	Amber	21.65	20.80	17.86	16.61
	Flint	16.81	15.59	13.59	12.37
Large scale	Flint	21.25	.....	.....	15.90

The ratios of alkaloids to other solids, *i. e.*, per cent of total solids minus per cent of alkaloids, are given in Table III.

TABLE III.—RATIO OF ALKALOIDS TO 100 PARTS OF OTHER SOLIDS.

Menstrua.	When Prepared.	After 3 Months.	After 8 Months.	After 16 Months.
U. S. P. XI	7.74	7.96	7.94	7.94
	7.76	8.24	8.97	8.86
U. S. P. X	7.21	7.53	7.53	7.54
Acetic acid (9%)	5.78	5.72	6.27	6.48
	5.76	6.02	6.82	7.38
	6.05	6.19	7.10	7.66
Large scale	6.03	....	....	8.01

DISCUSSION OF RESULTS.

The U. S. P. XI and U. S. P. X menstrua yielded elegant preparations which, over a period of sixteen months, lost 0.90 and 4.67 per cent of alkaloids in the case of the former and 1.21 per cent in the case of the latter; while the total solids decreased 3.29 and 15.5 per cent, respectively, in the former and 5.19 per cent in the latter. The preparations obtained using acetic acid (9%) lost 14.95, 5.00, 8.33 and 2.48 per cent of alkaloids; and 23.7, 23.3, 26.4 and 25.2 per cent of total solids, respectively.

No definite relation between loss of alkaloids and decrease in total solids is evident although in most cases the per cent decrease in total solids was roughly four times as great as the per cent decrease in alkaloids. The decrease in the per cent of alkaloids cannot be explained by occlusion or adsorption in the sediment, for while the sediment deposited in the last experiment with acetic acid (9%) was

next to the largest, the same preparation showed the smallest loss of alkaloids in that series. Light does not appear to have any particular effect on the alkaloidal content, but it appears to aid sedimentation. In all cases the ratio of alkaloids to total solids increased with time.

SUMMARY.

1. Ipecac preparations made by percolation with U. S. P. X and U. S. P. XI menstrua show little alkaloidal loss after sixteen months and deposit a small amount of sediment during the first two months after preparation.

2. Preparations made by percolation with acetic acid (9%) are not as stable as those prepared with hydro-alcoholic menstrua and should be prepared only for use in manufacturing processes.

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STABLE SUPERSATURATED SOLUTIONS OF CALCIUM GLUCONATE.[1]

BY GLENN L. JENKINS.

Various means have been developed to render supersaturated solutions of calcium gluconate stable. Heating in sealed ampuls (1) (2); the addition of alkali salts (3); the addition of boric acid or borax (4), (5), (6); the addition of aluminum chloride (7); the adjustment of the p_H of the finished product (8); and the addition of the soluble calcium salts of saccharic acid (9), mannonic acid (10) and lactobionic acid (11), (12) have all yielded products which have been used more or less in therapy. Numerous other compounds are reported in the references cited to produce some stabilization of supersaturated calcium gluconate solutions.

The observation that the calcium salt of methane disulfonic acid stabilized supersaturated calcium gluconate solutions led to the preparation and testing of a number of the soluble calcium salts of sulfonic acids. The salts prepared by heating the appropriate halide with an alkali sulfite and conversion of the product to the calcium salt included the calcium salt of: I, methane disulfonic acid (methionic acid) (13); II, ethyl sulfonic acid; III, ethane 1,1-disulfonic acid; IV, ethane 1,2-disulfonic acid; V, propane 1,2-disulfonic acid; VI, propane 1,2,3-trisulfonic acid and VII, benzene sulfonic acid (14). The average of two determinations of moisture at 180° C. and of two assays for calcium on the purified and dried salts are given in Table I.

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[1] Contribution from the Department of Pharmaceutical Chemistry of the College of Pharmacy of the University of Minnesota, June 15, 1937.

TABLE I.

	Compound.	Moisture %. Calc.	Found.	Calcium %. Calc.	Found.
I	$CH_2(SO_3)_2Ca.H_2O$	7.7	7.5	17.25	17.15
II	$(C_2H_5SO_3)_2Ca.2H_2O$	13.5	13.2	15.00	15.29
III	$C_2H_4(SO_3)_2Ca$	0.0	0.0	17.54	16.18
IV	$C_2H_4(SO_3)_2Ca$	0.0	0.0	17.54	17.32
V	$C_3H_7(SO_3)_2Ca.H_2O$	6.9	6.3	16.60	16.85
VI	$C_3H_5(SO_3)_3Ca_3.4H_2O$	9.6	9.8	15.78	15.61
VII	$(C_6H_5SO_3)_2Ca.H_2O$	4.8	4.5	11.30	11.14

The toxicity, hypercalcemia and irritant action of these salts compared to that of calcium gluconate, calcium lactate and calcium chloride were determined. The toxicity expressed as the minimum lethal dose in mg. per Kg. body weight was determined by intravenous injection into white mice. The irritant action and hypercalcemia were determined on dogs by intra-muscular injection in doses of 20 mg. of calcium per Kg. body weight, the volume of solution in each case being the same as for calcium gluconate and the blood calcium being determined at the end of one hour. The results are given in Table II.

TABLE II.

Compound.	Toxicity.	Increase in Blood Calcium, Mg. in 100 Cc.	Irritation.
Calcium gluconate	112.0	2.55	Slight
Calcium lactate	140.5	2.25	Marked
Calcium chloride	55.5	2.40	Severe
I	85.5	3.45	Slight
II	47.5	2.75	Severe
III	51.5	2.45	Severe
IV	68.0	2.80	Severe
V	53.0	2.60	Severe
VI	65.0	2.80	Slight
VII	50.0	2.30	Marked

The results indicate that calcium methionate is the best of the new compounds studied and that it is comparable to calcium gluconate as an agent for the increase of blood calcium. Calcium methionate having been found to be the best of the calcium salts of sulfonic acids studied, a further study of the value of this salt as a stabilizing agent for supersaturated calcium gluconate solutions was made.

The solutions were prepared by heating the required amounts of Merck's calcium gluconate which assayed 9.1 per cent calcium and calcium methionate which assayed 18.3 per cent calcium in sufficient water contained in calibrated flasks until solution occurred, replacing the water lost by evaporation, filtering through Jena No. 4 fritted glass and filling into soft glass bottles stoppered with rubber. Six bottles of each concentration of solution were prepared. Three of the bottles were kept in a room in which the temperature variations were approximately from 20° to 30° C. and three of the bottles were placed in a refrigerator which maintained a temperature of approximately 7° C. Observations of the solutions were made daily for 21 days and then at seven-day intervals for six months. The concentrations of the solutions and the time period during which two out of three samples deposited no crystals are given in Table III.

TABLE III.

Calcium Gluconate, Per Cent.	Calcium Methionate, Per Cent.	Days Stable, Room Temp.	Days Stable, 7° C.
5	1	200	200
5	3	200	200
5	5	200	200
7	8	200	200
10	5	11	14
10	10	200	193
10	12	200	200
10	15	200	63
10	20	200	182
10	30	200	175
15	5	7	0
15	10	8	1
15	15	49	56
15	20	119	77
20	10	2	0
20	20	35	8
20	30	17	28
25	30	28	6
30	35	3	1

Since one per cent of calcium methionate is equivalent to two per cent of calcium gluconate in calcium content, the data indicate that solutions which are stable and which contain an amount of calcium equivalent to from seven to seventy per cent of calcium gluconate can be prepared from the salts. Additional tests show that solutions prepared and sealed in ampuls are more stable than those in bottles. Solutions containing seven per cent of calcium gluconate and eight per cent of calcium methionate and solutions containing ten per cent of each salt when frozen in dry ice and allowed to thaw, yielded clear solutions. Other solutions of this concentration when agitated for five minutes each day for two hundred days showed no separation of crystals. Storage in amber bottles did not influence the stability of the solutions.

The stability of calcium gluconate-calcium methionate solutions does not appear to be influenced markedly by agitation, moderate changes in temperature or by light. Traces of extraneous matter which serve as centers of crystallization, such as sulfur from rubber stoppers, filter fiber, dust particles, and flaws in the glass of the bottle are the chief causes of instability.

SUMMARY AND CONCLUSIONS.

(1) Seven calcium salts of sulfonic acids have been prepared and tested for toxicity, production of hypercalcemia and irritation. It is shown that calcium methionate is the best of the salts studied.

(2) A study of the effect of calcium methionate in the stabilization of calcium-gluconate solutions has been made. It is found that solutions containing an amount of calcium methionate equal to or greater than the amount of calcium gluconate present yield relatively stable solutions containing the equivalent of from seven to seventy per cent of calcium gluconate.

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CONTROL OF SPECIALTIES AND NOSTRUMS IN PRESCRIPTION STOCK.*

BY JOHN F. MCCLOSKEY.[1]

Through the past centuries and up to the present time pharmacy has been confronted with many difficult and troublesome problems. Fortunately, when these problems are carefully considered and a clear understanding of the facts obtained, a solution is usually found; and when it is applied, generally the problem disappears and does not return, at least not in the same form.

The purpose of this paper is to present a very definite problem; one that is exceedingly complex and its ramifications are unbounded. Not only is the problem perplexing, but it has assumed the rôle of a profit-consuming Hercules. It demands attention and immediate action.

The title of this paper may indicate that the author has found a complete solution for the problem, but this is not so; the task is of such magnitude that it requires more than one brain and more than one solution. Nevertheless, definite suggestions are offered, mainly to promote discussion out of which may evolve some plan for control, as well as to guide those who may wish to follow them. I believe that if the suggestions were followed they would tend to lessen the severity and complexity of the problem.

The pharmacist has considerable difficulty in the control of his inventory relative to his prescription stock, mainly because once a preparation has been successfully introduced to the medical profession there follows an unlimited number of products that are similar, or, at best, just imitations of the original. Each of these products will have a group of followers made so by the extent of the advertising or the pressure of their salesmen. Naturally, it is expected that each of them will be stocked by the pharmacist.

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We are aware that medicine has been making rapid progress in the fields of preventative medicine and therapeutics. Consequently, if these organic and synthetic compounds, as well as the new specialties, keep on increasing, with their inevitable duplication, what is the pharmacist going to do about it?

In order to make the problem more specific and concrete, let us put it in the form of questions as follows: How may the pharmacist be guided in his acceptance or rejection of a new preparation which duplicates many products now stocked? Should he attempt to stock all items for which he has had a prescription? How may he control his inventory in order to conserve both space and cash? How can he inform the prescriber of the similarity of the product without harm to himself or to others?

Sad to say, but generally true, the physician will use and will prescribe those items which strike his fancy. His fancy is obtained and his good-will secured by plenty of samples, by the striking color combinations and the neat packaging. The compounds are usually quite presentable; if liquids, they are brightly colored and clear; if solid, the color combination or scheme still prevails; be it capsules, tablets or pills, running the scale from bright greens to all the hues of the color chart, while the ointments have nothing more as sales appeal than the collapsible tubes, and ampuls, their freakish forms.

In climaxing this campaign to put over a new product, and after allowing the advertising matter to get into the hands of its readers, there comes the suave, friendly, confidence-getting salesman. Since we have a tendency to run to titles, we call them "Detail Men," "Doctor's Contact Men" or "Medical Contact Men."

The pharmacists are required, or at least expected, to stock these items which in many cases are preparations "that have seemed beneficial" or "ought to be good." Sometimes they are the mass production results of some other physician's prescription that has in certain cases been successful and which is now offered to the public to cover all cases. Generally they are the official or the accepted standard formulas with a few inocuous changes such as color, or the addition of another medicinal ingredient merely to add distinction.

The responsibility for this condition cannot be placed upon either branch of the healing art. Pharmacy as well as medicine is to blame for the results.

Some physicians claim that the results of identical prescriptions vary in color, content and form to such an extent that they are forced even against their will to use standard manufactured preparations. This should not be true in so far as the U. S. P., the N. F. or the R. B. or other standard formulas are concerned, but it may be true when we consider the extemporaneous preparations made under varied conditions.

Again, because the physician is willing to use a coined word or a trade-marked word which is easily spelled, pronounced and remembered in preference to using the official titles, or, because he is not well grounded in Materia Medica and in prescription writing, or still further because he lacks the source of the common formulas. If this be so, then it is the duty of the profession as a whole to try and remedy this condition.

Mr. Frank A. Delgado estimates that about 125 new preparations are introduced each year and that only about 13% of them are extensively advertised. This

estimate is probably of a national scope, but how about the numberless ones that are put out each year and in every large city, that never get beyond the state lines?

Study the lists of the more reputable manufacturers and observe the formula in many of their specialities, study the lists of the less known and less reliable ones, and where possible, the formulas of their specialties. It will be amazing to see the multiplicity and duplications that occur and we are bound to arrive at the conclusion that the physician and the pharmacist are being exploited and forced to take all the risks and losses that occur.

Although the problem is serious enough to warrant attention and action at the present time, we must not become too greatly alarmed. In the "Professional Pharmacy," 2nd Edition, pages 39–41, it is shown that the official drugs, per se, still lead as ingredients in physicians' prescriptions; also that the combination or mixed prescriptions, that is, those in which the official drugs are used with specialties, are growing in numbers and hold a strong place in the total. The specialties alone average about 23% of the total of 8383 prescriptions that were studied.

This same source also disclosed that the cost of the specialties has a tendency to increase the cost of the prescription far above that of the officials. Nevertheless, there has been a steady trend toward the use of prepared products and, unless checked, the saying "bottle pourer and label remover" may become true.

Therefore, if the pharmacist is to have some control over his inventory in the prescription laboratory he should bear in mind that there are but four classes of remedies, *viz:*

1. The officials.
2. The open formulas of the reputable pharmaceutical houses.
3. The nostrums, which are secret formulas.
4. The "private" formulas which may be used in many ways both for good and for evil.

With the first there is but little criticism, but it is in relation to the remaining three that the following suggestions are directed.

1. A specialty or semi-proprietary should not be accepted by the physician or the pharmacist unless there is sufficient data available to fully inform him pertaining to its therapeutic value and possible reaction when in combination with other substances.

2. Any product that tends to be substituted for an official or a recognized standard formula should be rejected.

3. A product should be rejected if the price is unreasonably high as compared to products that serve a similar purpose.

4. The cost of the pioneering work should be borne by the producer and not by the pharmacist. To insure this, the product should be distributed by reputable wholesalers under agreement to accept for full credit unopened, unsold packages. If distributed direct, it should be on a consigned basis for some return agreement.

5. Information pertaining to the company producing the product should be readily available, such data as their reputation in pharmaceutical and medical circles, their methods of distribution, their program of advertising, their qualifications to produce and the conditions which surrounded production.

6. Unusual, rare and sporadic ailments do not warrant stocking new products.

7. By agreement among themselves, the pharmacists in certain areas may distribute the load of stocking new items. Jones may have the full line of ampuls; Smith, a full line of biologicals; Davis, certain new specialties; etc. Each of them would then act as a wholesaler to one another.

8. An accurate and careful annual inventory should be made. Those products which have not shown a stock movement during the year should be removed and placed in a "morgue" or returned.

9. Every item should show date of purchase, price paid and the source of the purchase.

10. It may be wiser to refuse some prescriptions for certain specialties than to suffer a loss when the demand ceases. If more pharmacists were to do this, the physician would find that prescribing them is of little avail, due to the difficulty in securing them; this would cause a demand for the better known standard ones.

THE PHARMACIST AND PARENTERAL SOLUTIONS.*

BY SISTER CRESCENTIA WISE.[1]

The rapid development of parenteral medication has brought about numerous problems. While manufacturing pharmacists have done much to render this form of medication safer and more convenient, most pharmacists outside the manufacturing field have been slow to accept responsibility for extemporaneous preparations of parenteral solutions. Since the need for much of this medication is of an emergency nature there seems no valid reason why the trained pharmacist, in either the hospital or retail field, should consider this work to be the sole responsibility of pharmacists in the commercial field.

If local irritation is to be avoided some attention must be paid to the tonicity of the solution.

Since all fluids and secretions of the body contain dissolved substances, in definite proportions, these solutions will exert a certain definite osmotic pressure which is uniform for each fluid. (Since this paper deals with parenteral solutions only, we will confine our attention to blood and lymph, though isotonicity is of equal or greater importance in solutions intended for use in the eye or nose.) If a solution is introduced into the circulation it may contain dissolved substances in a different proportion or of a different character from those of natural body fluids, hence it will have a different osmotic pressure. When a liquid has a lower osmotic pressure than the body fluid with which it is mixed it is hypotonic; when it has a higher osmotic pressure it is hypertonic; when it has the same osmotic pressure it is isotonic. Whether any given solution is isotonic depends upon (1) the proportion of dissolved substances which it contains and (2) upon the character of those substances. Salts which dissociate freely exert a greater osmotic pressure than those which dissociate slightly or organic non-dissociating substances. Therefore the type of dissolved substance is of more importance from osmotic pressure standpoint than the amount in solution.

The practical value of this subject lies in the fact that hypotonic or hypertonic liquids when injected into the circulation in considerable amounts, may cause pain until equilibrium is established between the osmotic pressure of the fluid within the tissue cells and that of the injected fluid. When only a small amount of solution is injected into the blood stream it is quickly diluted so that the difference is not felt.

Often a hypertonic solution is desired for therapeutic purposes but as a rule an isotonic solution is more satisfactory. If given subcutaneously any solution that is not isotonic will cause temporary local irritation.

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Systemic reactions do occur, unavoidably, occasionally. In our hospital, over a period of a month, there were slight reactions following 4% of the injections. This compares favorably with reports from other hospitals.

A survey of the literature reveals five main causes for systemic reactions.

1. Foreign protein.
2. Speed of injection.
3. Temperature of the solution.
4. Individual susceptibility and disease.
5. p_H of the solution.

Speed of injection, temperature of solution, individual susceptibility and disease are scarcely within the scope of this paper but it would be well to mention that numerous investigators have found that the more acutely ill the patient, the more likely is a reaction to follow an intravenous injection, and that in septicemia a reaction is a rule rather than an exception.

Foreign protein may come from water which complies with all the requirements for Aqua Distillata, U. S. P. Much stress has been placed upon double and triple distilled water. If these are available, well and good, but they are not important. One large eastern hospital has been using single distilled water for more than four years and has not had a single reaction that was not traceable to sources other than water. It is of vital importance that the still be in good condition and that the water be exposed to the bacteria-loaded air, as short a time as possible, and be sterilized at once after it is distilled. The bacteria, pathogenic or non-pathogenic, are killed by sterilization but the protein matter from their dead bodies remains in solution and causes at times very severe reactions. One writer has stated that it is not advisable to inject into the circulation a floating bacterial graveyard.

The p_H of the water should be very close to 7. Theoretically, water is neutral but in practice it is rare to find it absolutely so. A small percentage of CO_2 dissolved in it as the water condenses will cause slight acidity but this is not sufficient to cause any difficulty. If it is permitted to remain in contact with the air, it will absorb additional CO_2 besides becoming saturated with bacteria. These bacteria during sterilization break up and increase acidity. It is a good practice to have the inlet tube to the receiving flask pass through a plug of cotton so as to filter the air during the period of distillation.

The degree of acidity or alkalinity of the finished solutions is often of vital importance, and while the total acidity or alkalinity may be determined by titration, the true acidity should be ascertained by determining the p_H concentration. This may be very satisfactorily accomplished by the colorimetric method and in many cases by the use of nitrazine paper.

In regard to solvents, distilled water and physiological sodium chloride solution only, need be considered here.

The glassware used, flasks or containers, graduates, graduated pipettes or burettes, etc., should be of insoluble glass. An intermediate grade termed "harder than soft" has been used satisfactorily by one large hospital. It is advisable to treat all new containers, especially if made from the "harder than soft" variety of glass, by first sterilizing in them, Boric Acid Solution. This fixes the alkali in the glass.

The style of containers will depend upon individual preference. Hard glass bottles with skirted rubber stoppers are satisfactory for quantities up to 100 cc.

For quantities over 100 cc. convenient containers are bottles graduated from bottom to top and from top to bottom, closed with two-holed rubber stoppers. In one hole is a piece of glass tubing reaching nearly to the bottom of the bottle, an air inlet. The other hole is free to receive the glass connector and rubber tubing. A round piece of pure rubber is fitted over the stopper and over all is a metal screw cap. This provides a hermetic seal. Another advantage of these containers is that the danger of accidental contamination in transferring the solution from one container to another is avoided. Pyrex Erlenmeyer flasks may be used for any quantities. These should be closed with non-absorbent cotton wrapped in close mesh gauze which has been flamed to rid it of shreds and capped with cellophane paper which should come well down over the neck of the flask.

All new rubber parts should be given preliminary treatment before use. It is the practice in our hospital to allow new rubber to stand twenty-four hours in 2% NaOH. It is then thoroughly washed in running tap water and placed in distilled water where it remains another twenty-four hours, after which it is sterilized.

Filtration can be accomplished much more efficiently and rapidly if a little thought is given to the filtering media. The creped paper shreds, and, frequently, repeated filtration through the same paper only adds to the number of shreds in the filtrate and has the disadvantage of exposing the solution to the bacteria and CO_2 of the air over an unjustifiable period of time. Much less annoyance will be experienced if a hard smooth-surfaced filter paper such as Reeve Angel Close Texture Filter Paper (Reeve Angel Co.) or Whatman Filter Paper (Coleman Bell Co.) is used. A little difficulty may be encountered with viscid solutions. These may be filtered through a bed of siliceous earth in a Büchner funnel using suction, or a "fritted" glass filter may be employed. The latter has been satisfactorily used for some time at a certain University Hospital.

Many factors influence the stability of parenteral solutions. Reference has been made to p_H concentration as affecting systemic reactions. It also materially affects stability of solutions. Nearly every solution has its optimum p_H.

Solutions should be sterilized immediately after preparation. It is preferable to make the solutions from water distilled during the working hours of the morning rather than from sterilized distilled water. One filtration is avoided in this way and the water is fresher. All the solutions under consideration at this time can be sterilized in an autoclave at 15 or 20 pounds pressure for 15 minutes. A hypodermic needle may be inserted in the rubber caps, but if they fit tightly and the bottles are not more than two-thirds full this will not be necessary.

The hermetically sealed solutions have been proven to remain stable over a long period of time, but generally it is not necessary to use solutions which have been prepared longer than a week. Though the demand for parenteral solutions fluctuates it should be comparatively easy to keep sufficient solutions on hand without becoming overstocked.

Obviously not all solutions are suitable for preparation by the hospital or retail pharmacist, but there can hardly be any reasonable excuse for his feeling incompetent to prepare such simple solutions as Solutions of Sodium Chloride, Dextrose, Magnesium Sulfate, Physiological Buffer Salts and Fischer's Solution.

Sodium Chloride Solutions present no particular problem except freeing them from filter shreds and by observing what has been said above, this problem is easily

solved. As a rule chemically pure Sodium Chloride, reagent quality, should be used, but there is no objection to the use of Sodium Chloride U. S. P.

Physiological Solution of Sodium Chloride U. S. P. contains 8.5 Gm. NaCl dissolved in enough freshly distilled water to make 1000 cc. The U. S. P. directs that this be used within 24 hours unless hermetically sealed (rendered impervious to air or other fluids) in which case it shall respond to certain tests for sterility.

A hypertonic solution of Sodium Chloride between 5% and 10% is frequently called for and should be available. It would be practical to prepare a 10% solution in units of 300 cc. This could easily be diluted to any concentration less than 10% by introducing directly into the container through a sterile glass funnel the proper proportion of sterile distilled water. Then the solution may be administered from the original container, clamping off the rubber tubing when the desired amount has been given.

According to most writers Glucose Solutions require the use of chemically pure dextrose, though one very good authority uses Dextrose U. S. P. The concentrations in use at the present time are 5% and 10% dissolved in either distilled water or physiological salt solution and 50% dissolved in distilled water.

There is a great deal of discussion about the advisability of buffering dextrose solutions. Dextrose is normally acid and will deteriorate in alkaline solution. Unbuffered, it may have a p_H as low as 5.0 after sterilization, but this represents all available acidity. The buffer power of the blood is such that this degree of acidity can be handled, except in case of excessive depletion of alkaline reserve, in which case extemporaneous addition of alkali (buffer salts) is advisable. One reliable authority advises the routine use of Sodium Biphosphate U. S. P. (NaH_2PO_4) as a buffer. It is used in the proportion of 2 Gm. per 1000 cc. of solution and should be dissolved in the distilled water before the Dextrose is added. This maintains a p_H of 6.5 to 6.7. The literature lists no disadvantages in the use of buffers and its routine use seems logical until some practical reason for not using it is revealed.

The only problem in connection with the preparation of Magnesium Sulfate Solutions is the preservation of the chemical. The formulas are for the crystallized salt ($MgSO_4.7H_2O$). Either the C.P. or reagent grade should be used and should be purchased in glass containers to prevent loss of water of crystallization.

It is used in 50% and 25% solutions. The dosage is usually 2 cc. of 50% or 10 cc. of the 25%. These may be put up in convenient sized vials with skirted rubber closures. Care should be taken that the containers are not more than one-half or two-thirds full to allow for expansion in the sterilizer.

Physiological Buffer Salts may be prepared ready for use or in the concentrated form and diluted when ready for use. The formula for the concentrated solution is as follows:

Lactic acid 85%	1.2 cc.
NaCl	3.0 Gm.
KCl	0.2 Gm.
$CaCl_2$	0.1 Gm.
Distilled water *q. s.*	20.0 cc.

This must be diluted to 25 times its volume (500 cc.) before use.

In the preparation of Fischer's Solution the first step is to select a formula. Quite a number exist, each claiming to be the original. The following formula was supplied by Merck and Company:

NaCl	14.00 Gm.
$Na_2CO_3.H_2O$	4.33 Gm.
Distilled water *q. s.*	1000.00 cc.

Anhydrous or Crystalline Sodium Carbonate may be substituted for the monohydrated provided the weight is adjusted according to their molecular weights. C.P. salts should be used and it is essential that only *hard* glass be used on account of the alkalinity of this solution.

This solution presents some as yet unsolved problems. After 24 hours a precipitate forms so that the solution must be absolutely fresh. There could be no chemical reaction to explain the precipitate. It would be convenient to have a concentrated solution which could be diluted when needed, but a concentrated solution (the amounts in the formula in 100 cc.) yields a floating precipitate resembling a white membrane. Only a clear solution may be used.

The economy of preparing these solutions is shown by the following tabulations which are taken from a report of a North Carolina Hospital with the exception of the "units used" column in which is substituted the figures from the records of our own hospital.

TABLE I.—COST OF COMMERCIAL PRODUCTS.

Solution.	Cost per Unit.	Units Used.	Cost.
1000 cc. 5% dextrose in normal saline	$0.79	1325	$1046.75
1000 cc. 10% dextrose in normal saline	1.05	1325	1391.25
100 cc. ampul dextrose 50%	0.40	1200	480.00
50 cc. ampul dextrose 50%	0.23	1200	276.00
500 cc. physiological NaCl solution	0.32	7935	2539.20
			$5733.20

TABLE II.—COST OF SOLUTIONS PREPARED IN HOSPITAL PHARMACY.

Solution.	Cost per Unit.	Units Used.	Cost.
1000 cc. 5% dextrose in normal saline	$0.1823	1325	$241.5475
1000 cc. 10% dextrose in normal saline	0.2187	1325	289.7775
100 cc. ampul dextrose 5%	0.0505	1200	60.6000
50 cc. ampul dextrose 10%	0.0323	1200	38.7600
500 cc. physiological NaCl solution	0.0963	7935	764.1405
			$1394.8255

Cost of solutions prepared as above, includes cost of (1) chemicals, (2) water, distillation, depreciation of apparatus (still, etc.), (3) capping and (4) sterilization, depreciation of sterilizers and breakage of containers.

A glance at the figures shows that it costs less than one-fourth as much to make the solutions as it does to buy them from a commercial laboratory.

While the cost of ingredients is often passed on to the patient and therefore does not immediately concern the hospital, both physicians and laymen are taking notice of increasing cost of illness, and whatever is done to lessen the cost without lessening the efficacy of the treatment will be of direct benefit to the patient and indirectly will benefit the physician and the hospital. When nearly one-third of the total number of patients are either charity or only part-pay patients, as was the case in our hospital for the year 1936, the saving to the hospital would go far toward extending the works of charity in which those in charge of the hospital are intensely interested.

Even though intelligent and conscientious attention must be given to every detail from the time the preparation of parenteral solutions is begun until they are administered, still there is no reason why the trained pharmacist in the hospital dispensary or in a retail pharmacy should not be competent and willing to assume this responsibility.

WHY SIMPLE OINTMENT, U. S. P.?*

BY WILLIAM A. PROUT[1] AND JAMES R. ADAMS.[2]

Dispensing pharmacists are asking why we have Simple Ointment as it now appears in the pharmacopœia, when apparently it cannot be employed as a base in any of the official ointments, therefore why include it? With this question in mind, we began a study and comparison of the pharmacopœial ointments with regard to the constituents of their bases and the proportion in which they are combined. As a result we find a group of ten ointments, three of which have a base composed of constituents identical with those of Simple Ointment, six of which use yellow petrolatum in place of white, and seven of which use yellow wax in place of white. In none of the bases did the percentage strengths of the constituents in the bases vary more than one and one-half per cent in the case of wool fat and wax and not more than three per cent in the case of petrolatum, as is shown by the table following.

TABLE I.

Pharmacopœial Ointments.	Per Cent of Active Constituent.	Per Cent of Constituents Other Than Those in the Base.	Per Cent of Petrolatum.	Per Cent of White Petrolatum.	Per Cent of White Petrolatum if Simple Ointment Was Used.	Per Cent of Wool Fat.	Per Cent of Wool Fat if Simple Ointment Was Used.	Per Cent of Yellow Wax.	Per Cent of White Wax.	Per Cent of White Wax if Simple Ointment Was Used.
Boric acid	10	....	..	80	81.0	5	4.5	.	5	4.5
Tannic acid	20	Glycerin 20	54	..	54.0	3	3.0	3	.	3.0
Belladonna	10	Dil. alcohol 5	75	..	76.5	5	4.25	5	.	4.25
Chrysarobin	6	Chloroform 4	74	..	75.6	5	4.2	5	.	4.2
		Liq. petrol. 6	..	..	....	.	..	.	.	..
Nutgall	20	....	70	..	72.0	5	4.0	5	.	4.0
Ammoniated mercury	10	....	..	80	81.0	5	4.5		5	4.5
Yellow mercuric oxide	1	Liquid petrolatum 1	88	..	88.2	5	4.9	5	.	4.9
Iodine	4	KI 4	70	..	72.0	5	4.0	5	.	4.0
		Glycerin 12	..	..	....	.	..	.	.	..
Sulfur	15	. ..		75	76.5	5	4.25	5	.	4.25
Zinc oxide	20	Liquid petrolatum 10	..	60	63.0	5	3.5	.	5	3.5

Aside from the difference in the color of the finished product, bases made with yellow wax and yellow petrolatum in place of white wax and white petrolatum seem to be equally satisfactory in consistency.

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[2] Instructor in Pharmacy, Medical College of the State of South Carolina.

After making this comparative study, we feel that the variation in percentage strengths of the constituents of these bases is neglible. We find that we can make just as satisfactory products using Simple Ointment in place of the basal constituents as listed in the different monographs. For the convenience of the pharmacist who can make these ointments using a standard base, we ask the question: why cannot we have Simple Ointment as the base for the ointments in the Pharmacopœia as was done in previous revisions?

IODINE IN LIQUID PETROLATUM.*

ITS PREPARATION AND A METHOD FOR ASSAY.

S. W. BOWER AND LEWIS G. FREEMAN.[1]

The therapeutic value of Iodine in Liquid Petrolatum has long been recognized, but no satisfactory method of procedure has been advanced to obtain a solution, the definite strength of which may be reasonably certain in the finished preparation. The lack of uniformity of the product is largely dependent upon the method of dissolving the Iodine, also, the volatility of this element at room temperature requires extra precautions in effecting solutions. Furthermore, the time required for solution is governed by the viscosity of Liquid Petrolatum used. On account of these differences several questions arise.

How much Iodine is lost by the prevalent trituration procedure?

Is the often recommended addition of Potassium Iodide advantageous in effecting solution more rapidly and is the limit of solubility increased by this addition?

Is this limit of solubility the same in Light Liquid Petrolatum and Heavy Liquid Petrolatum?

Are the advantages of solubility obtained by any alternative method superior to solutions made by trituration?

Limited information is available on the physical constants of solubility of Iodine in Liquid Petrolatums. Clark (1) in 1919 reported the findings of the Chemical Laboratory of the American Medical Association, in which a saturated solution was equivalent to 1.4% Iodine. No statement of specific gravity and viscosity of the Petrolatums used in this experiment is given. Two kinds of Liquid Petrolatum are described in the U. S. P.—the Heavy Liquid Petrolatum having a kinematic viscosity of not less than 0.381 at 37.8° C., and the Light Liquid Petrolatum having kinematic viscosity of not more than 0.370 at 37.8° C. No limit is given for the specific gravity of each, but a range of 0.828 to 0.905 at 25° C. is the U. S. P. XI standard.

One commercial source supplies six grades having definite physical constants for both viscosity and specific gravity. They are according to trade names:

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[1] School of Pharmacy, Univ. of Buffalo, Buffalo, N. Y.

(x)	Liquid Petrolatum.	Specific Gravity.	Kinematic Viscosity.
1	Amsol	0.8900–0.9050	0.735–0.757
2	Soconol	0.8850–0.8950	0.702–0.724
3	Talcol	0.8750–0.8850	0.437–0.460
4	Amtol	0.8650–0.8750	0.301–0.324
5	Panacol	0.8600–0.8700	0.265–0.289
6	Comptol	0.8450–0.8550	0.156–0.182

(x) Furnished by Standard Oil Company of New York.

The label statements for the physical constants of the commercial available forms are either that of the U. S. P. limits or none at all. Greater detail of specifications are desirous for uniformity.

The only assay method given in the literature for Iodine in Liquid Petrolatum is that furnished by Clark (1), who uses chloroform to extract the Iodine from the Petrolatum and subsequently titrates with Sodium Thiosulfate solution using starch indicator. The end-point in this method is not sufficiently sharp due to length of reaction time of starch iodide—frequently requiring 0.3-cc. excess of Thiosulfate—therefore, back titration is necessary to avoid error.

The following method using alcohol for extraction was devised, so that the completion of the reaction is immediate and definite:

Transfer about 10 Gm. of Iodine in Liquid Petrolatum mixture, accurately weighed, into a separatory funnel. Add 25 cc. of ethyl alcohol and shake for one minute. After settling, draw off the lower layer into a second separator, shaking the Liquid Petrolatum mixture again with 25 cc. of alcohol. Proceed in this way until extraction is completed as indicated by a colorless Liquid Petrolatum. Usually four extractions are necessary. Rinse funnels with a little alcohol adding the washings to previous extractions. To the combined extracts, add 100 cc. of distilled water, 10 cc. of Potassium Iodide T.S. and with starch solution as indicator, titrate with $N/10$ Sodium Thiosulfate until colorless. Each cc. of tenth-normal Sodium Thiosulfate used is equivalent to 0.01269 Gm. of Iodine.

To serve as a check on this method, a concentration falling below the saturation point was prepared. In a tared volumetric flask a definite weight of Liquid Petrolatum was added to a previously accurately weighed quantity of pulverized recrystallized Iodine. After ten minutes of constant shaking, the container was placed in a water-bath at 80° C. for one-half hour, shaking intermittently. Complete solution resulted. Upon cooling to room temperature the preparation was assayed by the above method. From the weight of the Iodine and Liquid Petrolatum used, the per cent of Iodine recovered was calculated. The accuracy of this method is shown in Table I.

TABLE I.

Petrolatum Weighed, Gm.	Iodine Weighed, Gm.	Iodine Found, Gm.	Per Cent Iodine Recovered.
Sp. gr. 0.8506	...	...	...
89.73	1.0549	1.0526	99.78
97.40	1.1485	1.1460	99.79
93.27	1.0965	1.0914	99.53
103.50	1.2169	1.2205	100.30
Sp. gr. 0.8731	...	...	...
107.92	1.2360	1.2384	100.20

Saturation points of Iodine in seven different Liquid Petrolatums in which solution was effected by digesting the mixture for three hours at 100° C. resulted in variations from 1.32 to 1.42 per cent Iodine by weight as given in Table II.

TABLE II.

Oil.	Specific Gravity.	Per Cent Iodine.
A—P. D. & Co.—Light	0.8506	1.39
B—Comptol	0.8562	1.33
C—Amtol	0.8674	1.40
D—Commercial	0.8731	1.42
E—Talcol	0.8746	1.32
F—Soconol	0.8846	1.36
G—P. D. & Co.—Heavy	0.8886	1.37

Experiments were conducted to determine if the solubility of Iodine in Liquid Petrolatum is increased by the addition of Potassium Iodide. Using Light Liquid Petrolatum, Sample A, supersaturated Iodine solutions were prepared by heat to which 1% and 2%, respectively, of Potassium Iodide were added. The supernatant liquids on assay were equivalent to 1.389 and 1.40 per cent Iodine. Evidently the increase in solubility or as an aid to solution is not substantiated for Iodine in Liquid Petrolatum as is the case in alcoholic, hydroalcoholic and aqueous solutions.

Numerous difficulties are encountered in dissolving Iodine in Liquid Petrolatum by trituration, such as the volatility of the Iodine, differences in viscosity of the Liquid Petrolatum and time required to make solution. Appreciable variations in strength result, depending upon the method of procedure used in effecting solution. The prevalence of triturating Iodine in Liquid Petrolatum is no reason for its continuance, especially when the volatility of the element at room temperature means loss in the finished preparation depending upon the length of time required. This loss, using different viscosities of Liquid Petrolatum, may be greater than imagined. Even though great care may be employed in weighing the small quantity prescribed, the procedure can defeat the obtaining of a uniform, accurate product. Justification of this was found by having the Senior Dispensing Class prepare one-fourth to one per cent solutions of Iodine in Liquid Petrolatum of one- and two-ounce quantities. In no case was solution effected in less than ten minutes and upon assay the Iodine in the resulting product was equivalent to 40–75% of the quantity weighed.

Further recheck of this student contribution was made using 0.065 and 0.130 Gm. of Iodine in 30 cc. of Liquid Petrolatum, Samples A and D. From the figures given in Table III, it is evident that quantity, time and viscosity are variables

TABLE III.

	Iodine Weighed, Gm.	Kind of Oil.	Quantity, Cc.	Trituration Time, Minutes.	Iodine Recovered.	Per Cent Iodine Recovered.
(x)	0.065	A	30	5	0.0532	81.85
(x)	0.130	A	30	11	0.0993	76.38
	0.065	A	30	11	0.0475	73.08
	0.065	A	30	12	0.0456	70.16
	0.130	A	30	20	0.0798	61.40
	0.065	D	30	20	0.0418	64.31
	0.130	D	30	30	0.0608	46.78

(x) Chloroform dispersion.

which prevent an accurate product. It is interesting to note that several drops of chloroform used in pulverizing the Iodine previous to adding the Liquid Petrolatum decreased the trituration time and reduced the per cent loss in the finished product.

In order to overcome these difficulties the following method is recommended. Heat the Liquid Petrolatum contained in a glass-stoppered bottle to 70° C. in a water-bath, this requiring 6 to 7 minutes. To this heated oil on the water-bath add the prescribed amount of Iodine. Complete solution is effected requiring five minutes for one-quarter per cent to 23 minutes for one per cent. The apparent loss as given in Table IV may be explained by the smaller amount of Iodine weighed. It is evident that both compounding time and accuracy are gained.

TABLE IV.

Iodine in Preparation, Gm. per 30 Cc.	Time on Water-Bath 70° C., Minutes.	Iodine Recovered in Solution, Gm. per 30 Cc.	Per Cent Iodine Recovered.
0.065	6.5	0.0631	97.2
0.065	7.0	0.0648	99.8
0.130	11.0	0.1267	97.5
0.130	11.0	0.1281	98.6
0.195	17.0	0.1916	98.3
0.260	23.0	0.2579	99.2
0.260	23.0	0.2561	98.5

When such solutions are made on a water-bath using screw-capped bottles, the assay shows 15–20% Iodine loss in the solution which was found deposited on the cork or alkali liner at the top of bottle. This shows the necessity of using only a glass-stoppered container in preparing solutions of this nature.

SUMMARY.

1. A method for assaying Iodine in Liquid Petrolatum is presented.
2. The saturation point of Iodine in Liquid Petrolatum ranges from 1.32% to 1.42% controlled by the viscosity of the Liquid Petrolatum.
3. The errors in trituration procedure are demonstrated.
4. An accurate method for incorporating 1/4–1% of Iodine in Liquid Petrolatum is given.

REFERENCE.

(1) Clark, Albert H., JOUR. A. PH. A., 8, 611–615 (1919).

DEVELOPING THE PROFESSION OF PHARMACY THROUGH THE HOSPITAL.*

BY DON A. BROOKE.[1]

To every registered druggist who is a college man there should be two main objectives in his relation toward pharmacy: *First*, to establish himself as a professional man in his community; *second*, to raise the standards of Pharmacy to a level with that of the allied professions, *i. e.*, Medicine, Dentistry and Nursing.

This can be accomplished in the smaller cities or towns of 10,000 to 20,000 through the local hospital. In the smaller cities especially, the hospital is regarded

* Presented before the Sub-Section on Hospital Pharmacy, New York meeting, 1937.

[1] Pharmacist, Hastings, Nebr.

as the most professional place in town, and any druggist connected with it is regarded by the public as a professional pharmacist. Furthermore, a hospital of 100 beds or less is hardly able to hire a full-time registered druggist and must, therefore, look to some local store or stores for its prescription orders.

Realizing this, and knowing that giving hospital service would promote intra-professional relations, I went to the Superintendent of Nurses in our town and offered to give one or two hours per week, teaching in the Hospital Nurses Training School. Nearly all of the local doctors were giving considerable time during the school year toward this work, and I felt that Pharmacy should also be represented. The Hospital Board welcomed my suggestion and I was assigned to teach "Drugs and Solutions" and "Materia Medica" two hours per week throughout the school year. I will say that the first year certainly took a lot of outside time, but the hospital people seemed well satisfied and it was of great educational value to me also; in fact, it was like going to college all over again. It also proved a great help to our drug business, in that, after the first year of teaching, the hospital turned over practically all of their drug and biological business to our store.

Furthermore, the teaching of the student nurses classes not only gives you a professional standing with the nurses, but gets most of their drug business during their training period and also after they graduate. After a nurse graduates and goes on private duty, her recommendations go a long way in deciding where the patients will buy their sick room supplies.

But, after all, it was neither the hospital nor the nurses which proved the greatest benefit to me as a pharmacist; it was the medical men themselves. In this particular hospital the staff is made up of practically all the local physicians and dentists, and during the school year staff meetings are held each month to discuss case histories and other things pertaining to the hospital. As a member of the teaching staff I have made several informal talks to these doctors on Pharmacy problems, and last season I was given ten or more minutes at every staff meeting to talk on drug medication. This I did in a somewhat different way than drugs are taught in either Pharmacy or the Nursing Schools. Each month I made an outline of different official drugs and proprietary remedies that are given for the same bodily condition or disease, *i. e.*, drugs used somewhat for the same thing therapeutically. For example, last winter I gave a talk on anti-anemic drugs, on vitamin products, on urinary antiseptics, on hypnotics and on sedatives. This winter I expect to prepare outlines on the new National Formulary syrups for vehicles, on anti-acids, on barbitrates, on heart remedies and anthelmintics.

These outlines consist of the official preparations and the leading proprietaries that are prescribed. I try to give a true comparison as to their relative therapeutic value, their composition and appearance, and the relative cost of each to the patients. These outlines are copied on the blackboard before the staff meeting and copies are given to the doctors who desire them. I was surprised at how much the doctors appreciated these outlines and the explanations that I gave with them. The detail men only give their own particular remedy for a certain condition, and the physician has no way of getting a comparison of values and costs of all the well-known remedies for the same disease.

This raises the druggist's prestige with the medical men, besides encouraging them to write better prescriptions. Of course all of this teaching and making out-

lines takes considerable time and study, but one who is genuinely interested in pharmacy will be well repaid, both by the increase in the ethical part of the drug business and the personal satisfaction which comes from knowing and promoting the professional part of the pharmacy profession.

PHARMACIST—PHYSICIAN RELATIONSHIP.*

BY CARL A. ABEND.[1]

It is with temerity that I submit myself to the profession while I reopen a maltreated chronic abscess. I speak of the much feared ghost in the closet of every hospital pharmacist—the elusive phantom of "coöperation between pharmacist and physician."

Grant me the right to remove the dust-laden scabs that have formed over this chronic wound that seems incapable of healing with a firm and healthy base.

Grant me the right to declare that until the pharmacist can shake himself from the lethargy and routine of compounding he will continue to occupy a small part in the functioning of institutions for medical care, institutions whose very reputations are in his hands.

Other than continuing in name, many institutional pharmacists have steadily receded from the central activities of their organization. They have lost the dignity of being thought of as part of the staff. They have lost the property of forming the smooth unifying synaphes between the patient and doctor. They have lost the ability to insert their arts and their sciences into the routine of the practitioner in such manner as to make the practitioner conscious of their efforts.

The pharmacist of altogether too many institutions has allowed himself to slip away from the field of active productive effort and has metamorphosed into a simple shopper of drugs, a pharmaceutical Shylock, whose greatest professional effort obtains in the arithmetic of counting tablets and measuring liquids. To-day's pharmacist has lost much of the old time luster that was his, he has lost a certain something that heretofore signaled to the world that the arts and sciences he practiced fell under the heading of a profession, and not just a job.

The entire fabric of any institution can be refined and perfected if effort is made for the closer coöperation between pharmacist and physician. I need not indicate that I have reference to professional and not personal coöperation. There are examples of such typical coöperation sufficient for reference.

Let us concede that each hospital, regardless of size, has certain peculiarities in its management or in the make-up of its staff that may make the establishment of close harmony difficult. But even with this concession there are ways and means of developing this to-be-sought-for goal.

At the Grace Hospital in Detroit the pharmacist is present as a member of the Staff Medical Meetings and all Clinical Pathological Conferences, together with the Clinical Director, the Chief Resident Physician and the active heads of the medical and surgical staffs. Once a month he is given the opportunity of recapturing a privilege long usurped and all too often abused by the contact and detail men from

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[1] Chief Pharmacist, Grace Hospital, Detroit, Mich.

the large pharmaceutical houses. He, the pharmacist, and not the peddler, attempts to give to the staff and resident interns a short, concise and absolutely unprejudiced opinion of all worth-while pharmaceutical preparations brought to commercial markets. The pharmacist, and not the detail man, attempts to give a reliable report as to the pharmacologic and therapeutic properties of these newer products.

By the expenditure of some little extra effort the pharmacist should be able to present pertinent information of a similar kind with respect to U. S. P. and N. F. preparations. This information or review is of especial importance at times following the decennial revisions. Beyond the chemical and pharmacologic estimation of such preparations the pharmacist should have nothing to say. Matters of clinical application or success are strictly out of his domain.

With one eye to the future we have tried out a new routine at the Grace Hospital this year. I propose to briefly outline this innovation.

Through affiliation with the Wayne University College of Medicine we assume teaching responsibilities for four senior medical students each month. These students are guided through various activities of the hospital and two days of each week during the four they are placed under the tutelage of the pharmacist. An attempt is made to inculcate respect for the knowledge and responsibility of the man who compounds the prescriptions they will shortly be writing.

In the few hours they have available an attempt is made to exhibit the actual and practical aspects of our profession. Each student is given twenty prescriptions as originally used by Dr. Bernard Fantus of the Illinois College of Medicine. They are asked to familiarize themselves with these standard prescriptions and to give especial attention to the nature of vehicles and flavoring agents employed. Much stress is placed upon these seemingly unimportant features of prescription writing.

Following these activities the students are given problems in percentage solutions and dilutions. It is remarkably shocking to note evidence of the average senior medical student's inability to execute simple problems in such matters. Such a time is particularly fitting to demonstrate to these young physicians how much they take for granted in writing their orders and how much they lay bare their reputations to the pharmacist.

Along practical lines they are taught the rudiments of making ointments, mixtures, capsules, collyria, ampuls, etc. They are taught to recognize good, bad and indifferent products. These same principles are applied in the matter of the several pharmaceutical classifications. The last period of the month is spent in reviewing official doses and portions of the text of the U. S. P. and N. F. in such a manner that they learn to appreciate them in the same way as they do when they think of Osler's Medicine or Babcock's Surgery.

Out of a successful year's experience, it is my opinion that such a plan is feasible wherever a hospital and medical school are in close proximity. It is also my firm belief that work along such lines is capable of creating and maintaining closer and better relationship between the physician and the pharmacist.

It is my earnest belief that along these lines of endeavor there lies a vast amount of constructive influence that institutional pharmacy has been altogether too wont to neglect. Such neglect fosters an insidious degradation of a powerful bond between the physician and the pharmacist. Properly expended effort, how-

ever, will nurture a reliance by the physician and surgeon that is professionally satisfying. You will find as time passes not only that your long lost sense of self-esteem is returning, but also that you yourself are firmly cemented in the center of the very pulse of every professional activity in your institution. Is not this the position we have trained ourselves to assume?

HOSPITAL PHARMACY AND ITS RELATION TO RETAIL PHARMACY AND MEDICINE.*

BY MORRIS DAUER.[1]

For many years the excellent, useful, highly dignified and ethical services of the American hospital pharmacist have not received the recognition to which they are justly entitled and which they so rightfully deserve.

The light of this faithful public servant, "the hospital pharmacist," has been hidden under a bushel. The contributions which he has made to professional pharmacy and medicine by virtue of his liberal professional education, followed by the subsequent training which he has gained from the older practicing pharmacists and added to that vast storehouse of knowledge which he has constantly been gaining as the years have gone by, actually sacrificing his early youth and middle age, a sacrifice indeed for the benefit of public service and public health protection and ultimately serving his state and his country, have received little recognition from hospital executives and his brethren who comprise the pharmaceutical fraternity.

It has been the impression of some of our unenlightened hospital executives that a hospital pharmacist needs but a vague outline of pharmaceutical education and training, and as the speaker experienced while discussing professional pharmacy with a hospital executive who naively said "You are always talking about professional pharmacy. What's so professional about pharmacy? All you have to know is a set of weights and measures. You take a list of ingredients that appear on a doctor's prescription, you throw them together, shake them up in a bottle, and you have a mixture." Alas! this medicus is not the only one who has this erroneous impression and it is the duty of the hospital pharmacist who comes in contact with such individuals to use intelligent measures to correct this misconception and leave in its place an indelible impression that pharmacy is an exact science requiring in its own field prescribed courses of study and training under a well-qualified faculty of a recognized university or college, which is further supervised by the various boards of higher education which regulate very strictly this profession just as the medical education is directed and supervised.

In order to advance the interests of hospital pharmacy and in order to clarify this situation, the speaker has prepared and delivered several lectures before the Interne body of Kings County Hospital, the institution where he is serving as Chief Pharmacist. In addition to resident and visiting staff physicians and surgeons, the attendance from this association was surprisingly large. In these lectures I strove to inculcate into their minds the use of our official preparations, either in whole or in part. During one of my lectures I discussed the official vehicles,

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[1] Chief Pharmacist, Kings County Hospital, New York City.

also coloring and flavoring ingredients which they could use in their prescriptions so as to render them palatable and pleasing to the senses of sight and smell. This lecture was entitled "Aromatics and Coloring in Prescriptions and Their Psychological Effect on the Patient." During the course of this lecture, I exhibited various distasteful drugs. These drugs and the coloring and flavoring agent were exhibited in glass-stoppered bottles bearing glass labels. Every means was employed to lend an air of professional pharmaceutical dignity.

The listeners were given samples of the crude materials to taste and then a flavored mixture containing the same ingredients, so that they would be able to make comparisons.

A strenuous attempt was made to distract their interest from proprietary preparations of a secretive nature, and light was focused on professional pharmaceutical preparations prepared by the hospital pharmacist, emphasizing that in spite of the numerous attempts to divorce entirely the practice of medicine from the use of the official drugs and preparations, the physician in active practice sooner or later reconciles himself to the part played by these drugs in his fight at the bedside of the patient.

The hospital pharmaceutical department must always serve as a lecture hall wherein the pharmacist in charge must lay the foundations of future contacts between the doctor and the pharmacist. The pharmacist must forge an unbreakable link between the allied professions of medicine and pharmacy.

History reveals that the pharmacist of ancient and medieval times was the pioneer to systematize the treatment of the sick and ailing. Gathering the various herbs, roots, barks and other vegetative matter, he, by the aid of crude utensils, compounded mixtures of these organic ingredients and prepared them in a suitable form for human administration. Although tried in a rather empirical manner, eventually some system of use was devised at last. With the advancement of the healing art, there can be no room for doubt but that the pharmacist, like a well-trained soldier in the army of public health protection, has kept in step with all modern discoveries and advances made to the goal of highest degree of refinement in the rationalization of the treatment of the sick.

The pharmacist employed in a hospital can do much to facilitate the institution of a pharmaceutical economy program which will reduce substantially the expenditures for drugs, medicines and biological products.

Paramount in this economy program is the formulation and presentation by the Chief Pharmacist, in coöperation with the chiefs of the various services of the medical and surgical staffs, of a medical formulary which will be given to the members of those staffs consisting of a complete catalog of prescriptions and formulas so varied as to include all sub-divisions of medicine; including such important specializations as Cardiology, Dermatology, Gynecology and Obstetrics, Otology, Pediatrics and Internal Medicine.

The hospital physician and intern must be reached by the hospital pharmacist before the detail man of the patent medicine firm succeeds in hypnotizing them by means of cosmetic pharmacy, which includes the use of fancy names, gaudy packages, highly colored capsules and glowing description of the infallibility of his wares. After the physician has enjoyed the song and dance, the poor patient and pharmacist must pay the fiddler.

The ultimate aim of the hospital pharmacist and his Formulary must be to familiarize the physician with proper prescription formation so that when he himself is in private practice he may employ a number of palatable and receptive preparations, the composition of which he is thoroughly familiar with, to the advantage of himself, his patient and his pharmacist.

I am offering as an example of a hospital formulary, a manual which I have edited and compiled entitled, "The Medical Formulary and Prescription Manual." This book was officially approved and adopted by the Department of Hospitals on September 13, 1934, and is now being used in all 26 municipal hospitals in the City of New York. "The Medical Formulary and Prescription Manual" comprises approximately 957 separate and distinct formulas embracing pharmaceutical preparations employed in every branch of medical science.

I have supplemented every prescription in the book with a note giving the physical characteristics and properties of each prescription, thus acquainting the doctor with the color, odor and taste of any prescription which he may select. This data is not found in any other book, to my knowledge, published in this field.

In the preparation of this book, economy without sacrifice of therapeutic efficiency, was always a paramount issue. With that end in view, I have developed a considerable number of medical and surgical preparations designed to replace expensive preparations which had been and were being used in the Department of Hospitals. This innovation did not only result in a tremendous saving but rid these preparations of their secretive nature and resulted in uniform compounding and dispensing methods.

To convince and to stimulate an everlasting admiration of the results of the skill and art in the practice of Pharmacy, I prepared a permanent exhibit of every preparation as set forth in this book; this exhibit to exemplify the use to which these preparations can be put to the best interest of the patient, his physician and his pharmacy.

I have watched with keen interest and gratification, the numerous embryo medicos who have come here, absorbed the atmosphere of professional pharmacy as practiced in a hospital and have gone forth into private practice taking these ideals with them. They now possess a knowledge of sound professional and ethical pharmacy and a sincere appreciation of the necessity of a closer friendship and cooperation between themselves as physicians and their colleagues, the pharmacists, on the neighboring corner behind the colored show globes.

May I, at this time, urge in all sincerity the closest coöperation between the young physician and the neighborhood pharmacist. The two are indispensable to each other. The pharmacist should always be the friend of the physician, always ready and willing to extol his virtues and minimize his faults, ever bespeaking the best that can be said of him who is seeking to establish a practice and reputation.

MUST A PHARMACIST BE A PSYCHOLOGIST?*

BY ALICE-ESTHER GARVIN.[1]

This topic was selected in order to learn what we may do to correct some of the evils, not in sales psychology, but in the pharmacist's knowledge of himself. Why, for example, did you select your family physician? Because he lives near you? Because you went to school with him or because of his reputation? Why does a customer select a particular pharmacy? Because it is near him? We know perfectly well that many people walk past six or eight stores in order to reach the one they have selected. Why? What has one store, or one pharmacist, that another lacks? They may all have graduated with honors from a college; passed the State Board examination with superior grades; been an officer of a local or state group. Why is one selected and the other passed by? Of course we hear a lot about service so I won't mention it except to say that I believe there is such a word. I'm going to deal with the more intangible topic, personality.

What for example, does it profit a man to have a beautifully lighted, streamlined, meticulously clean store, and then to forget that his coat hasn't been laundered for a week, and he hasn't shaved since day before yesterday? Has a well-worn blue sweater any place in a Prescription Department? It seems a little incongruous, but women customers are fastidious, and in the stores where they trade they demand cleanliness. How about the smoking of cigars or cigarettes while compounding prescriptions? I've seen men do it; so have you. The radio, gaily emitting a dance tune which the pharmacist hums while glancing at the ingredients specified on the physician's blank, does not add to any customer's confidence. Nor does the carrying on of a conversation with a pal while a woman is waiting for the medicine, and the pharmacist is talking to some one else about the National League, or the stock market, or a party that has gone or is coming. It is decidedly unflattering to any person who is buying, for instance, a clinical thermometer, to have the pharmacist say, "This is a very fine one—what time did you get in last night, Tom? Two fifty. What did your wife say about that?"

Another feature which takes customers past your store is its being used as a rendezvous for your family. I can think of some stores, at the moment, where wife, brothers, father, mother, move right in at 11 A.M., sit at the fountain or at a table, and remain there until closing time. I have seen the proprietor's wife nursing the baby in the prescription room; I have seen a daughter washing the family poodle there. Meals are served, cards are played. The place for one's family and friends is away from one's place of business.

We encourage the doctors to be our customers, and then we greet them with "Hello, Doc.!" than which there are few greater insults. No physician likes to be called "Doc.," and those of you who are Doctors of Philosophy or Doctors of Pharmacy will admit that you prefer the entire title. . . . . We do a lot of talking about back to Pharmacy, or on to Pharmacy, or whatever you prefer, and then we sell ourselves short in what it takes. We need discipline in our stores; a clerk should never, no matter how well he knows the manager or proprietor, call him by his first

* Presented before the Section on Commercial Interests, A. PH. A., New York meeting, 1937.

[1] Secretary, Connecticut State Pharmaceutical Association.

name when customers are present. A pharmacist, even in the neighborhood stores, should try to avoid the "Hi Babe, how ya doin'?" Our stores need dignity and discipline; so do our clerks, and so do many of us. Where can we learn it, and how can we teach it? The kind of psychology that a pharmacist needs is, "Know Thyself."

THE IMPORTANCE OF THE ALLIED PROFESSIONAL SERVICES TO THE PHARMACIST AND TO THE COMMUNITY.*

BY JOHN N. MCDONNELL.[1]

The pharmacist has a two-fold duty in the proper practice of his profession. Although the chief function of the pharmacist, that phase of his practice that has been handed down to him through the centuries, has been to supply drugs and medicaments to the public for the cure of disease, there is a secondary service required of him. This may be best expressed as "the duty to impart information regarding the preservation and betterment of the public health."

The pharmacist is the community information bureau in matters pertaining to the above. He is closer to the layman than the medical, theological and law professions. Laymen know the pharmacist best; they trust him and they believe in him. They feel free to place their confidence in him, for they feel that they understand him and he, them.

Much has been said in the past regarding the many phases of diversified activity that make up the proper conduct of prescription pharmacy practice. Service to the physician, better comprehended as a means of greater coöperation between the professions, includes far more than is included within the scope of prescription compounding alone. Service to the community, inextricably bound up with the pharmacist's service to the medical profession, finds its outlet in efforts on behalf of the public health and welfare, and in a large measure, brings unexpected monetary returns to the dispenser.

PREVENTIVE MEASURES.

With the rapid development of preventive medicine, as a result of the discoveries in the field of the micro-organisms, there has arisen a greater appreciation of the important place pharmacy holds in the public health field. Preventive measures are not a recent innovation for since the dawn of civilization wherever people have gathered, there strict regulation has been propounded for the protection of the general welfare. During the past years, as science discovered ways and means whereby bacterial infectious diseases might be combated, medicine fought the battle and pharmacy supplied the weapons. Now, we are called upon as never before to aid in the eradication or alleviation of all diseases, contagious or otherwise, serious or simple, wherever they appear, and to provide against recurrence.

A century ago, the age span of man was approximately forty years. To-day it has increased to nearly a decade and a half more than that figure, and the emphasis in the planning and building of hospitals has swung to hospitals for the

* Presented before the Section on Commercial Interests, New York meeting, 1937.

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older people, rather than infants and children. We are laying stress on immunization to-day, and the comfort and convenience of the patient.

An evidence of this change may be found in the recently launched campaign against venereal diseases.

ANTI-VENEREALS.

The pharmacist holds an important place in the public health control of these diseases, for they are the most difficult to bring to light and the hardest to trace to extermination. By consulting the corner druggist, the public makes its first tentative attempts at medical treatment. The average citizen feels more at ease discussing such misfortune with him. In his hands is placed an awful responsibility for we know that the control of syphilis, gonorrhea and related conditions depends chiefly on early diagnosis and treatment.

The pharmacist should stress the importance of immediate medical treatment, and refer the patient to the nearest physician or clinic. The layman is prone to consider a few doses of an anti-syphilitic sufficient, and the pharmacist can do no better service to the commonwealth than to insist on prolonged treatment. Inadequate treatment of these diseases has caused more unhappiness and destruction to the common good than many wars.

BIOLOGICALS.

Along with the subject of preventive medicine and immunization are the biological products. The handling of these products gives a very definite responsibility to the pharmacist. In recent years, the federal government has seen fit to place rigid supervision over the manufacture and distribution of all biological products under the direction of the United States Public Health Service, while the pharmacist, an individual, is entrusted with the preservation and dispensing of such material.

It is commonly understood as essential that anti-toxins, serums, vaccines, etc., must be stored carefully at proper temperatures to prevent deterioration. Unfortunately, some pharmacists do not appreciate their duty. As evidence of the average lack of intelligence along this line, a recent survey of 1600 drug stores in a great city revealed that slightly less than one-half of these establishments kept biologicals in cold temperatures. Thirty some odd per cent kept them in soda fountain cabinets, at least satisfactory, though not very professional. Less than 16 per cent possessed special refrigerators for biological items. Of the latter group of pharmacists rendering satisfactory service, less than one-half of them used the refrigerators for other drug, chemical and dietetic products which are required to be kept in low temperatures. Thus, only one in every six pharmacists knew and cared enough about his practice to keep biologicals under optimum conditions and only one in every twelve knew enough to preserve all of his medicinals under proper conditions. All of the druggists carefully watched the expiration dates of the biologicals, yet how many of the negligent fifty per cent knew of the extent of deterioration of the products stored faultily during the time?

TREATMENT OF SICK.

Aside from the problems of preventive medicine, we must consider that primarily, the drug store exists for the purpose of providing for the public those articles

which are required for the treatment of the sick. There is more to the practice of pharmacy than the compounding of prescriptions or the mere purveying of unrelated merchandise. Since the key-note of the modern pharmacy is "service," the pharmacist is expected to not only be able to instruct the public how to use that appliance or medicament that is purchased from him, but also be able to give to the public some pertinent advice as to the best particular type of instrument or medicament adapted for the special purpose for which it is intended.

This logically includes not merely drugs but also all that information necessary for the public's intelligent use of those drugs; the various apparati which are used for the application of the drugs or other remedial agents, such as heat or cold; the various instruments and utensils which are used in the sick room; and the facts relative to the prevention of the spread of disease to others not previously infected. Together with the foregoing, we have the need for disseminating necessary information relative to the needs of the communities' babies, the expectant and nursing mother; the service of the diabetic patient; vitamins and vitamin products; infants' and invalids' foods; the public laboratory services in assistance as clinical pathologists to the allied professions, public health examinations, commercial testing and the examination of foods; the home medicines and the medicine cabinet; first aid in emergencies and public health work; the allied legitimate products such as trusses and orthopedic aids, spices and food flavors, and cosmetics and non-allergic preparations; and the information services which cover the library and literature, the proprietary medicines and their intelligent distribution, and community and personal care.

NEGLECT.

The student is taught in college in his pharmacy course, the physical and therapeutic properties of drugs, not in order that he will usurp the physician's function of treating the sick, but so that he may intelligently aid the medical practitioner. If a knowledge of how drugs act is a desirable thing, how equally important is an acquaintance with the construction, purposes and method of use of these drugs and appliances so frequently required in the management and prevention of disease. Unless the pharmacist knows how to properly use these apparati, it is obvious that he cannot properly serve his customers.

Unfortunately, this important subject has been generally neglected in the colleges of pharmacy. It has remained for the pharmacist to learn all valuable information in his years of later practice. In the past three years, some few institutions have seen fit to add such instruction to their curricula. Partly set between the theoretical and the operative sides of pharmacy, this subject is neither, yet draws equally from both. With the ever-increasingly important place which the pharmacist is being called upon to take in the defense of the community's health, this phase of his pharmaceutical education is being more appreciated by the practicing pharmacist.

SICK ROOM APPLIANCES.

The logical point of departure in a consideration of this phase of the pharmacist's activities is to select the so-called "sick room appliances" because of their actual relation to the compounding and filling of prescriptions for ill humans.

Wherever there is a physician's prescription, there is a definite need for an appliance of this type.

In many cases the patient may be already fortified with all of the necessary impedimenta of the sick room. If the pharmacist is not positive whether or not the patron is supplied, he should ask and strive to provide the necessities solely in the interests and welfare of the ill one.

Few pharmacists are sufficiently aware of the importance and scope of these supplies and their manifold types and uses. Most pharmacists are content to merely have something "that will do," rather than that which is best indicated. Some few pharmacists have developed these services to the utmost, and those have found the return more than ample. Unfortunately, a great majority of the druggists of the nation, whether through indolence, through lack of a desire to provide satisfactory service or through unsatisfactory preliminary training, have failed to provide even an adequate amount of this material to their communities. The following table, compiled from a survey conducted some few years ago in an eastern city, showed a woeful percentage of stores with satisfactory service, for while the survey was unfortunately brief and does not include such indispensable items as bedpans, urinals, sputum cups and many other similar items, the low percentage of pharmacies carrying such vitally important items as applicators, depressors, etc., is truly amazing. The survey revealed the following:

	Stores Carrying Items in Stock.	Stores Carrying an Adequate Stock.
Bandages, gauze, cotton, etc.	100 per cent	88 per cent
Sponges	100 per cent	85 per cent
Finger cots	94 per cent	80 per cent
Suspensories	90 per cent	70 per cent
Vaccination shields	90 per cent	70 per cent
Eye cups	90 per cent	80 per cent
Vermin exterminators	90 per cent	80 per cent
Eye and Medicine droppers	85 per cent	75 per cent
Corn plasters, etc.	80 per cent	70 per cent
Gloves, rubber and surgeons	80 per cent	45 per cent
Eye shields	70 per cent	40 per cent
Lamb's wool	65 per cent	45 per cent
Lint	60 per cent	40 per cent
Crutches	56 per cent	40 per cent
Wrist Bands	50 per cent	40 per cent
Corn files	50 per cent	20 per cent
Applicators	50 per cent	45 per cent
Depressors	50 per cent	45 per cent
Medicine glasses	40 per cent	35 per cent
Stomach pump	25 per cent	25 per cent
Elastic stockings	16 per cent	8 per cent

That even fifteen per cent of the stores do not stock such obviously important items as medicine droppers and eye droppers, seems incredible. Ten per cent without eye cups and one-fifth of them without corn plasters or rubber gloves is almost unbelievable. It is a sad commentary and an indictment on the state of pharmacy to-day and an obvious explanation of the reason why druggists fell so in the esteem of the allied professions.

It has been estimated that there are approximately 170 millions of prescriptions filled annually in the United States, valued at a total of 150 millions of dollars. We know that less than seven per cent of the total number of pharmacies provide approximately three-quarters of this service, and it has been also estimated that there are 200 millions of dollars worth of appliances and professional supplies sold in the same period by the same pharmacies, the unit sale being greater and the proportionate return greater. That the pharmacist benefits in rational proportion is evident, for it is well known that the mark-up on products of this nature is at a 40 per cent on the selling price minimum. Of even more importance in our opinion, and aside from the economic angle, is the direct bearing this service holds in supplying necessities for the preservation of the public health.

BABY SUPPLIES.

Another phase of the subject of professional service is to be found in the pharmacist's aid to the baby, to the nursing and to the expectant mother. This is one of the newest and more emphasized of drug services and presents excellent opportunities for a combination of professional knowledge, service to the community and merchandising ability.

It has been found that in 41 per cent of all American homes, babies are to be found ranging from birth to ten years of age. In other words, in every 515 homes (for that is the average number of homes per drug store), 212 have baby residents in this age group, totaling 466 in all as an average. Each baby consumes on an average $40.00 per year in medicines and supplies, being a total of $18,640, which should be the average income of the druggist for the babies in his community. If he does not service this evident demand, some one else is, and he is failing in his duty. In this classification come baby foods, which require a complete understanding of their composition and use, sundries, medicines and drug needs, and toiletries. A great deal of emphasis has been placed in recent years on this subject and we may pass on.

DIABETES.

Another source of revenue, and a demand for scientific knowledge and service, is the diabetic. Once a diabetic, always a diabetic, and the pharmacist should better appreciate him as a consistent patron. Insulin, food scales, diet books, nutritional products, clinical apparatus and sugar-testing outfits, and syringe outfits find an outlet.

VITAMINS AND FOODS.

The amount of misinformation prevalent regarding the vitamins is astounding, and the pharmacist may well render an immediate and valuable service to his community by regulating intelligently the use and abuse of these organic catalysts. Since no provision has been made to confine these potent and powerful vitamin preparations to the prescription laboratory, we must assume the task of educating the public.

What are the vitamins? What do they do? How are they standardized and where are they to be found? When do we need them? What is vitaminosis and how is avitaminosis brought about? The public is conscious of the importance of these questions and expects the pharmacist, who is the scientifically trained pur-

veyor of these products, to protect them from their own ignorant abuse of these products. Infants' and other special foods assume increasingly important places in the modern pharmacy as we follow the advance of the sciencelet, Nutrition. Are we prepared to present essential facts pertaining to it?

Along with the above we may add specialized medical service, such as the presentation of veterinary medicines, especially those for cats and dogs, household pets being an important part of family life in every part of the country. The development of this phase of your service, prompted by local life and practices, is an important move. Dental and osteopathic medicines are others.

PUBLIC HEALTH ACTIVITIES.

Supplementing all the above services is the last, and most important, of the pharmacist's duties: that of the intelligent distribution of authentic information to his patrons. Proprietary medicines govern many laymen's therapeutics, and must be purveyed with discrimination by the pharmacist. By rendering an information service about the latest developments in medications, therapeutics and scientific thought, he may materially aid doctors and dentists, as well as himself. The pharmacist's library should be a factor to his pharmacy, not an appendage.

CONCLUSION.

This lengthy, and somewhat elaborate discourse has been intended to focus the attention of pharmacists upon their possibilities. No pharmacy may measure up completely to this yardstick. If pharmacists consider each of these phases, recognize their importance to the public, and appreciate the opportunities for profit contained in them, every one will benefit. Many of pharmacy's ills may be directly traced to our laziness, lack of enterprise and desire to scrap with a competitor over non-professional competitive lines.

More originality in operation and more emphasis on service to the community should be the aim of to-day's pharmacist. Without further thought, great returns will come unheralded in real and psychic income.

FAIR TRADE—PAST, PRESENT.*

BY SAMUEL SHKOLNIK.[1]

The fair-trade movement, aimed at curbing loss-leader selling and predatory price cutting, is now well established and definitely accepted. The legislatures of some thirty-eight states have decided on the desirability of fair-trade legislation and the so-called fair-trade movement. The Supreme Court has spoken on the constitutionality of it. Now, let us analyze just how it has operated and how it is going to operate, what part the manufacturer and wholesaler have played, will play and must play, and what part the retail druggists have played and must play.

Past Is Cited.—We all know that the predatory price-cutting evil reached its peak during the past two decades and the years of depression. It was during those

* Presented before Section on Commercial Interests, New York meeting, 1937.

[1] Legal counsel for the Illinois Pharmaceutical Association and Instructor in Pharmacy and Business Law at the University of Illinois College of Pharmacy.

years, when volume of sales had reached its lowest ebb, that there was a drastic effort on the part of every manufacturer, in order to survive and in order to satisfy stockholders and creditors, to boost the volume of sales, and that resulted in drives to increase sales. In order to do so, it was necessary for them to play the cards as the purchasers of their merchandise, particularly the large organized distributors, wanted them to play. It was not that manufacturers wanted to see the small retailer driven out of business, but to maintain their balance sheets on the black side and to distribute the output of the production departments it became necessary for their sales departments to make concessions—willingly or unwillingly. However, the more they played into the hands of unethical retailers and organized distributors, the more pronounced became the demand for special allowances and secret rebates, requiring a still more intensified drive for volume to compensate for the loss in margin of profit, until it reached a point where the manufacturers themselves could not cope with the situation any longer. During this frenzy of volume distribution they could not afford to effectively consider, less so enforce, retail price stabilization or price maintenance, even if they could legally do so. In the meantime predatory price cutting was threatening the survival of the independent retailer who was not "in" on any of the special buying concessions.

NRA Era.—Then along came the NRA and temporarily saved the manufacturers from the embarrassing problem of controlling retail prices. Generally speaking, under the NRA and the drug code promulgated thereunder, the manufacturer was saved the fight of prohibiting distribution of commodities, at retail, at less than the wholesale list price. With the collapse of the NRA, the problem again became a serious one, and manufacturers were called upon once more to tackle it in some intelligent and effective manner. The organized retail industry demanded it and, the manufacturers not being able to cope with the situation, our lawmakers were contacted. Retailers began to demand some form of legislative action to keep them in business, and the Fair Trade Act was one of the laws sponsored in practically every state legislature.

Supreme Court Decision.—Let us observe just what the title of the fair-trade act provides. We read that it is an act to protect trade-mark owners, distributors and the public against unfair trade practices and predatory price cutting. However, the momentous United States Supreme Court Fair Trade decision disregards, apparently, the plight of the retailer—at least fails to recognize it—and simply declares that the primary aim of the legislation is to protect the trade-mark, brand or name of the producer and that the price restriction program, which is the fair-trade contract program, is merely a means to an end. We, as retailers, were celebrating the victory, but our Supreme Court did not say that the small retailer must be perpetuated in business. There is not even any dictum in the decision where the plight of the independent retailer was taken into consideration or into account.

Artificial Picture.—That is where the fallacy of the whole thing lies. We are not sailing under true colors. If we need legislation to keep us from being extinguished from the business world, then the legislation should be direct. If it is a legislative public policy to perpetuate the existence of small, independent druggists, who serve their community unselfishly, why do we have to sail under the pretext of protecting some one's trade-mark? There is something artificial about the structure. Why advocate the Fair Trade Acts as a manufacturer's aid? Why at-

tempt to defend them from the attack that they are price-fixing statutes and will cause increases in prices of nationally advertised items? Why not advocate and defend them on the ground that they promote fairer and cleaner competition and democracy in business opportunity, eliminating dishonest and predatory business abuses which tend toward monopoly, and thus perpetuate in business the hundreds of thousands of small, independent merchants. Agricultural and industrial tariffs have been passed to aid the farmers and manufacturers, at the cost of higher prices. Why not do the same for the struggling retail distributors? Their turn is long overdue. It would also seem that the slight increase in prices of nationally advertised items is insignificant when compared with the value of the existence of the independent retailer—the backbone of the American community. Unquestionably, the small retailers are entitled to protection even at a small increase in cost to the consumer.

Manufacturers' Attitude.—So much for past history. Now let us ask some pertinent questions: Are the majority of manufacturers really and sincerely behind the fair-trade movement? Are they anxious to operate under fair-trade contracts? In securing the passage of fair-trade laws, how many manufacturers appeared before the legislative hearings in the various states and before the congressional committees considering the Miller-Tydings Bill, to urge the passage of fair-trade legislation? Inventory your experiences and consult your pharmaceutical press and you will come pretty close to the answers. It is a well-known fact that independent retailers, and not manufacturers, are primarily responsible for the passage of all fair-trade acts. Why is it necessary for your fair-trade committees to keep continually fighting with manufacturers' representatives to come under the fair-trade act if it is an act intended primarily to protect the manufacturers' trade-mark? I believe that the manufacturers are still bewildered by the unanimity and tone of the unexpected Supreme Court decision as well as by the terrific force of the country-wide Fair-Trade hysteria; and a good many of them just cannot make up their minds which way to turn.

"Domestication" Not Necessary.—We were told by a goodly number of manufacturers that the reason they cannot come under the fair-trade act, or operate under the fair-trade act, is because it would require domestication in every state where fair-trade acts are in operation. But that is incorrect. The plaintiff in the Illinois Seagram case was the Seagram Distillers Corporation, a Delaware corporation "licensed" to do business in the state of Illinois—not "domesticated" in Illinois. The Seagram Distillers Corporation did not distil whisky and did not own the trade-mark of the Seagram whisky. The Seagram Distillers Corporation was a separate and distinct "wholesaling" corporation purchasing the whisky from Joseph E. Seagram & Sons, another separate and distinct "distilling" corporation, not operating in Illinois. Joseph E. Seagram & Sons, the distillers, the manufacturers, the owners of the trade-mark, were not a party to the suit. They did not enter into fair-trade contracts. The wholesale firm, Seagram Distillers Corporation, the plaintiff in the suit, did enter into fair-trade contracts and did sell in Illinois. And our Supreme Court upheld the wholesaler's right, the Seagram Distillers Corporation's right, to protect the minimum fair-trade contract price of the whisky.

The Joseph Triner Corporation was the plaintiff in the second Illinois suit, involving Schenley Whisky products. The Joseph Triner Corporation is a Chicago

wholesale liquor concern. That corporation does not own the Schenley trade-mark but is engaged in marketing Schenley products. The Supreme Courts of the state of Illinois and of the United States held that, as a wholesaler, the Joseph Triner Corporation had a right to protect the minimum fair-trade contract retail prices and the trade-marks of the Schenley brands of liquor.

Dr. West's Case.—The recent decision of the Wisconsin Supreme Court in the Weco Products Company case, which relates to direct Manufacturer—Retailer contracts rather than Wholesaler—Retailer contracts, is even more conclusive on the subject. In that case the Court upheld the right of Weco Products Company, an Illinois corporation "licensed" (not "domesticated") to do business in Wisconsin, the plaintiff in the suit, to protect the good-will of the trade-mark "Dr. West's" used by it in connection with the tooth brushes and tooth paste which it produces and markets, and held that it is entitled to an injunction restraining a Wisconsin price-cutter from advertising or selling "Dr. West's" products below the minimum prices provided for in outstanding fair-trade contracts in Wisconsin covering same, even though the price-cutter is not a party to such contract and notwithstanding the fact that the plaintiff ships its merchandise to Wisconsin from Illinois—interstate—and is not "domesticated" in Wisconsin.

Fair-Trade Contracts.—Apply the principles of these decisions to our fair-trade problem, and you find a perfect set-up with or without the Miller-Tydings Bill. Under the two Illinois decisions, there is nothing to prevent any wholesaler in Illinois, or any other fair-trade state having a similar law, from entering into fair-trade contracts covering any and every commodity which bears a trade-mark and is in free and open competition with commodities of the same class produced by others, regulating the minimum resale price of that commodity, whether the manufacturer wishes it protected or not. Indeed a paradoxical situation may arise if a wholesaler should enter into fair-trade contracts providing for the minimum resale price of a commodity contrary to the wishes of the manufacturer thereof. If in a suit to enforce such wholesaler's fair-trade contracts, the manufacturer should intervene and assert its stand as being opposed to the price-restriction plan, what would the decision of the Courts be? While it is unlikely that a manufacturer would risk taking such a stand openly, it remains for the Supreme Court to have its final say on it, if, as and when it comes up. And under the Wisconsin decision there is nothing to prevent any manufacturer of a branded competitive commodity from entering into fair-trade contracts covering same even though such commodities are shipped in interstate commerce and the manufacturer thereof is not domesticated in the particular Fair Trade state.

Miller-Tydings Bill.—These remarks would not be complete if I did not touch upon the recent developments in the Miller-Tydings bill. That bill, as you know, was reported on favorably by committees of the House and Senate, and was to come up for a vote. Its passage was almost a certainty until the presidential stop order was announced. There have been some speculative rumors and guesses as to what prompted the presidential action, but one guess is as good as another. The administration economists have another side to concern themselves about—the consumers' side—which we, as retailers, in our sincere effort to extricate ourselves from the burdens placed upon us by the predatory outlets, are prone to underestimate, if not overlook. I wonder just how much effect the insistence by so many of

the fair-trade committees on the so-called $33^1/_3$ per cent mark-up had on the opinion of the administration economists and on the presidential stop order? Even though we assume that a $33^1/_3$ per cent mark-up is needed, that is an average mark-up, and by an average mark-up we do not mean a mark-up of $33^1/_3$ per cent on the fast moving items. The term average presupposes, of course, some figures below and some above, and which products should be sold below the average if not the products for which manufacturers have created a public demand, which require no professionalism to sell and for which we assume no responsibility to society.

Coöperation Essential.—Failure, if any, encountered in the practical operations of the Fair Trade Act, is due chiefly to misunderstanding, uncertainty, lack of co-operation and novelty of the plan rather than any fallacy of the Fair Trade principle. In order to have it operate smoothly and efficiently, a sincere effort is required on the part of each branch of the industry, although it would seem that there is now no moral force left to appeal to. Branches of industry are fighting just as much as governments all over the globe to perpetuate their own existence. Each industry is struggling to get along, even though it must do so at the expense of others. That only means that our responsibility as an organization is still greater. But what can we do?

Retailers' Duty.—What is our duty to the manufacturers? We cannot continue to enjoy the benefits, reaping the harvests of the fair-trade victory without being called upon some day to pay the fiddler. Do you suppose that the activities of certain department stores in telling the public that the fair-trade act means increased prices to the consumer on nationally advertised items are bound to boost the sales of the patent medicine manufacturers? Definitely not. Such activities, coupled with extensive clever advertising of competitive items, cannot help but decrease the sales of the patent medicine manufacturers. Under such a program, consumer resistance is bound to be built up.

Maybe manufacturers generally will not realize it until six months or a year or two from now. Maybe some others will not dare to say anything about it until six months or a year or two from now, although they will realize it long before. But how long can we expect them to tolerate it? I believe we are headed right now toward the very thing which is being inaugurated in some of the states, and that is "concentration week" drives. Every week, perhaps, we may be expected to do something for a manufacturer who has fought our battle, who has sacrificed his own volume to protect retail prices on well-advertised, rapid-turnover products, so as to increase our profits or at least keep them at the same level. Unless the majority of the independent retailers get "actively" behind those who are trying to help them in carrying along the fair-trade fight, we may expect to see the defeat of the entire program.

Enforcement.—It would seem highly advisable that retailers, and particularly retailers' associations should keep their hands off the enforcement of the Fair Trade Act and contracts. Remember, the title of the act and the reasoning of the Supreme Court in upholding the act deal directly with the protection of the trademark of the owner or producer of the commodity and not with the perpetuation of the small retailer in business, although that may be written between the lines and may have had a very important bearing upon the court's decision.

Let us not encourage consumer opposition and wholesale revolution against retail groups organizing to enforce fair-trade legislation. If the manufacturer does it or if the wholesaler does it, the consumer cannot point his finger and say, "The druggists got together. They had the bill passed in the legislature and are now trying to enforce higher prices on trade-marked commodities." Let them rather say, "The manufacturer is trying to uphold his good name, his reputation and the trade-mark which is so significant of the origin of his product, of the quality of his product and guarantee of the continuity of that same quality and nature of the product." That is the substance of the act that is the substance of the decision, and the enforcement should be pivoted around the wording of the act and the spirit and language of the decision; otherwise, we may be treading on unsafe grounds. If any action is to be taken by a retailer, it must be by an independent retailer, whose business is being crushed by unfair methods of competition, but not by an association of retailers.

MOTIVATING THE COURSE IN MATERIA MEDICA.*

BY VICTOR LEWITUS.[1]

The writer, who has been teaching Materia Medica and Toxicology for the past ten years, passes on the following material for what it is worth to those who may find something of value in this method as securing motivation for one of the major subjects in the pharmaceutical curriculum; namely, Materia Medica.

The student who begins a new course, has a right to know why it is placed in his program; and the novel method here proposed attempts to point out one way in which the student, by his own findings, can answer the question. This system has been employed by the writer in his recitation classes for the past seven years with apparent success. The difficulty of determining to what extent such a method is successful, is obvious to the experienced teacher of the subject.

It might be pointed out at the outset that this method is applicable to other fields or subjects than those herein mentioned; the method of attack being the important point of consideration for this article.

The first week that the class meets in the recitation, a discussion of the purpose of studying Materia Medica is initiated. There follows more or less of a "free for all" debate, and no particularly definite conclusion is reached, since where liberal discussion is permitted (as it should be) there are often as many "pros" as "cons;" and this is exactly the basis of the psychology which enables the writer to carry out his experiment, or rather to create the desire in the students to test out their several contentions.

Sometimes it takes the first two recitations to convince the class that experimentation is necessary (the term "experimentation" applying to a testing out of one's convictions to see whether they be true or false).

At the opportune time (this varying with each class as has been indicated) the following table is given to the class as an assignment to be brought in the following week:

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* Presented before the Section on Education and Legislation, New York meeting, 1937.

[1] Instructor in Materia Medica, Columbia University, College of Pharmacy.

Name..... Date..... Hours.....Store Location.....

Customer Number.	Pharmacy.	Chemistry.	Materia Medica.	Remarks.

The details of carrying out the assignment are as follows: "Take a long sheet of paper and copy the above table upon it. Take it to the store in which you work, and in case you are not regularly employed obtain permission to remain in some store for one evening or one day. If you are employed, let the data be gathered for one whole day, or if you work in the evenings for one whole evening."

The following details explain the columns listed in the table. The one listed Customer Number should represent the number of consecutive unselected customers as they come in to purchase something at the drug counter such as drugs, prescriptions, sundries, etc. Sales at other counters such as cigars, cigarettes, cosmetics and soda fountain (except such as require a knowledge of some phase of pharmacy such as preparing a castor oil "cocktail" at the fountain) should not be recorded in this study. Were this a special study of commercial pharmacy *all* of the transactions that occur within the store might have been included.

The column listed Pharmacy, represents any operation or transaction which requires a knowledge of prescriptions, their writing, interpretation or manufacture; the manufacture of preparations outside of prescriptions themselves; and commercial pharmacy, such as knowledge of costs, correct selling price, etc. Obviously, there is seldom a case where commercial pharmacy does not enter into the picture. However, there are some exceptions to this statement, namely, the rendering of "first aid" to the injured, giving advice as to dosage of some medicine that had been dispensed at some previous occasion, or answering some general question that does not involve the passing of currency.

The column listed Chemistry, represents any operation or merely theoretical knowledge of chemical processes or reactions involved in prescription manufacture or other pharmaceutical operations, an understanding of the chemical properties and solubilities, as well as a knowledge of chemical incompatibilities.

Under the heading of Materia Medica, such things as checking of dosage on the prescription, watching therapeutic incompatibility, general questions on the part of the customer regarding "how to take" the medicament or how to apply same; and anything related to a knowledge of Toxicology is included.

The last column, reserved for Remarks, is for the purpose of having the student make any special notes to substantiate his memory in case some point comes up in the future class discussion regarding the details of a certain transaction or sale; or in case a special situation presented itself.

A few random samplings of some of the assignments that were handed in by the students will serve to clarify the method that students employed in obtaining their records:

Name: (Student A. W.) Date.: Sept. 1932. Hours: 8–12 P.M. Loc.: N. Y. C.

Customer #.	Pharmacy.	Chemistry.	Materia Medica.	Remarks.
1	/		/	Lady wanted to get cough syrup to bring up phlegm.
2	/		/	Sold fountain syringe; lady wanted instructions.
3	/		/	℞ calling for Tr. Opium. Large dose; called up physician who changed it to Tr. Opii Camphorata.
4		/		℞ for $KmnO_4$ and glycerine. Dangerous to triturate hard.
5			/	Man bought 4 oz. Elixir I. Q. S., wanted to know use.
15			/	Lady wanted something for rough hands. They get sore after washing.

Name: (Student A. C.) Date: October 5, 1933. Hours: Full Day. Loc.: N. Y. C.

3			/	℞ as to dose.
9			/	Rhubarb and Soda, asked dose.
11	/			Made Boric Acid Ointment.
14			/	How to use calomel tablets.
16			/	How to use Spirit of Nitre.
19			/	Fever thermometer, how to use it.
21			/	10% Argyrol, how to use it.

Name: (Student S. C.) Date: October 1, 1933. Hours: 8–12 P.M. Loc.: N. Y. C.

10			/	Mineral oil, dose asked.
11		/		Saturated solution of potassium iodide.
13	/			℞ eye salve.
25			/	Nasal atomizer, use demonstrated.

Name: (Student P. J. A.) Date: October 5, 1933. Hours: Full Day. Loc.: N. Y. C.

2	/	/		How to mix $CuSO_4$ and Lime as insecticide?
5	/		/	How much Senna and manna must be given as a laxative?
7	/	/	/	How much aspirin can be taken without injury?
11			/	Is overdose of Bromo Seltzer bad for heart?
22			/	Is dried raspberry good to cure colds?
31			/	How much lysol can be used for antiseptic?

Name: (Student M. R.) Date: October 5, 1933. Hours: Full Day. Loc.: N. Y. C.
(NOTE: This was a hospital pharmacy.)

6	/		/	Dose digitalis tablets.
13	/	/	/	Fowler's Soln., the cautioned dose.
14			/	Use of witch-hazel asked.
21	/	/	/	Con. sulfuric—poison and asked use.
33	/	/	/	℞ acid and alkali incompatible.
39	/	/		℞ soln. ammon. acetate.
46	/		/	Thermometer, how read.
48	/		/	Basham's mixture, dose and use asked.

In the above tables, customer numbers omitted in this report purchased items such as toothpaste, milk of magnesia, epsom salts, etc., without any questions being asked. To save space, these items have been deleted from the student's report by the writer.

For those students regularly employed, this assignment does not entail much difficulty, except in a very busy store. It has been found that this problem may be solved by asking the "boss" to coöperate in the survey (which many of them did with much enthusiasm and interest). For those not working, other students in the class arranged to invite such individuals to their store to make the survey. In any case the student who never worked in a drug store as yet, was asked to seek the coöperation of the neighborhood pharmacist who, in most cases, was ready to allow an evening's study to the pupil. It might be pointed out, incidentally, that in a few instances students received employment as a result of this assignment.

It will be noted that the frequency with which the checks occur under the Pharmacy column refers to the price, though at times it undoubtedly occurs because of a strict knowledge of some pharmaceutical operation. The checking of one, two or all three columns varies with the nature of the items sold. It is this feature which adds interest to the study for the student.

Since this is actually a rough survey of the nature of drug store sales, and since these transactions vary with the neighborhood, time of day, the season and even the weather, the careful observer will immediately see that the results cannot be strictly interpreted. Furthermore, the variations due to the student's viewpoint as to what belongs under each of the columns in the above table, adds inaccuracies; but since this is not a quantitative study and chiefly qualitative in its aspects, the accuracy is not at all essential. The primary object of such a study is to point out that Materia Medica and related theoretical subjects, as taught as part of the present-day pharmaceutical curricula, are abundantly used in a practical way each day of the year.

It is not necessary to compare results of one column as compared to another, such as comparing Pharmacy and Chemistry, or the latter with Materia Medica, since this is not at all a "competitive" study. However, such a study would be very interesting to make, and with modified methods of gathering the data, might prove valuable.

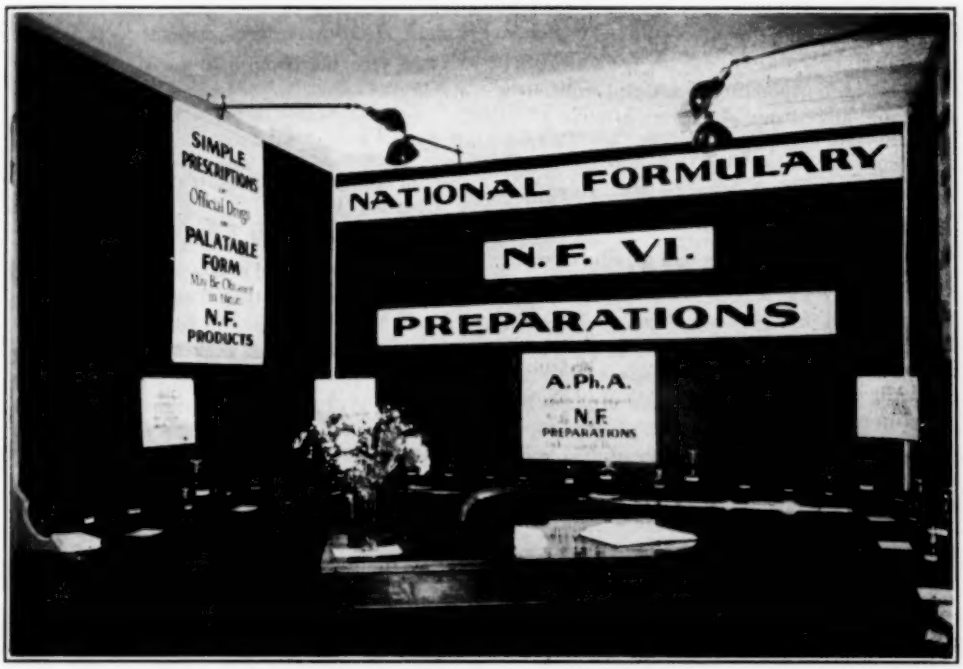
After the tables are completed and handed in, it has been the experience of the writer that the student shows much surprise at the amount of theoretical knowledge he is called upon to apply to his daily occupation or prospective vocation; in fact, the longer the previous experience of the student in the drug store, quite often, the more surprised he is at the results, for he did not realize how much or how often he really was called on to apply his knowledge of Materia Medica.

This experiment serves to convince the Pharmacy student of Materia Medica that the theoretical subjects within this department are not so theoretical after all. He discovers this by virtue of *his own findings!* It adds greater impetus to the desire on the part of the student to study the subject; or where there is not initial desire, it often creates one. It might further be pointed out here that in several instances the "boss" helped the student to gather the data, which in itself attached some importance to the experiment that was carried out by the student.

No better method has so far been devised, as far as the writer knows, which will motivate the student of a pharmacy school in the direction of the so-called theoretical subject of Materia Medica or its allied branches.

NOTE: The designation / signifies a check mark.

THE AMERICAN PHARMACEUTICAL ASSOCIATION EXHIBIT AT THE AMERICAN MEDICAL ASSOCIATION CONVENTION, SAN FRANCISCO, CALIF., JUNE 13TH TO 17TH.



Popular N. F. VI vehicles were featured. Those shown were Syrup of Glycyrrhiza, Syrup of Cherry, Syrup of Acacia, Syrup of Cinnamon, Aromatic Syrup of Eriodictyon and Isoalcoholic Elixir. Quart-glass-stoppered bottles were used to show the syrups. A four-ounce glass-stoppered bottle of each syrup was used for tasting purposes by the visiting physicians. Small glazed paper tasting spoons were furnished for each interested visitor.

The ten prescriptions, following, were exhibited as representing finished products employing the above-named vehicles. The prescriptions were numbered and a card carrying the same prescription number gave the Ingredients, Quantity, Directions and Use. Two bottles were prepared for each prescription, one for display and one for tasting purposes. The new easy pour, screw-cap prescription bottles were used. Paper of two sizes was handy on the desk for physicians to make notes.

"Notes for the Physician from the N. F. VI, No. 8," was given to each visitor. The exhibit proved very popular, many physicians tasting, asking questions and copying the prescriptions.

A portion of the exhibit was transferred to Oakland, June 19th to 22nd, for the California Pharmaceutical Association Convention. The Isoalcoholic Elixir and Syrup of Cherry were featured items at this Convention to acquaint the pharmacist with the proper technique in filling prescriptions calling for Isoalcoholic Elixir.

The exhibit was in charge of Prof. Julian M. Wells of the College of Pharmacy, University of California, under the general direction of Prof. Troy M. Daniels, and assisted by Mr. B. J. Kingwell.

℞ 1.

Potassium Bromide	30 Gm.
Distilled Water	30 cc.
Syrup of Glycyrrhiza, *q. s.*	120 cc.

Sig: One teaspoonful in glassful milk after meals and at bedtime. (Nerve Sedative.)

℞ 2.

Ammonium Chloride	10 Gm.
Syrup of Glycyrrhiza, *q. s.*	120 cc.

Sig: One teaspoonful in half glassful of water every two hours. (Expectorant.)

℞ 3.

Iron and Ammonium Citrate	10 Gm.
Distilled Water	5 cc.
Syrup of Cherry, *q. s.*	120 cc.

Sig: Teaspoonful to tablespoonful in water three times daily after meals. (Hematinic Tonic.)

℞ 4.

Diluted Hydrochloric Acid	10 cc.
Syrup of Cherry, *q. s.*	120 cc.

Sig: Teaspoonful in wineglassful of water three times daily after meals. (Digestant in Hypochlorhydria.)

℞ 5.

Urea	15 Gm.
Syrup of Cherry, *q. s.*	60 cc.

Sig: Teaspoonful in water every three hours. (Diuretic.)

℞ 6.

Syrup of Ephedrine Sulfate N. F. VI	60 cc.

Sig: One teaspoonful in water. (Antispasmodic.)

℞ 7.

Iron and Ammonium Citrate	10 Gm.
Distilled Water	10 cc.
Syrup of Cinnamon, *q. s.*	120 cc.

Sig: Tablespoonful in water three times daily after meals. (Hematinic Tonic.)

℞ 8.

Urea	15 Gm.
Syrup of Acacia, *q. s.*	60 cc.

Sig: Teaspoonful in water every three or four hours. (Diuretic.)

℞ 9.

Strychnine Sulfate	0.015 Gm.
Aromatic Syrup of Eriodictyon, *q. s.*	60 cc.

Sig: Teaspoonful three times a day after meals. (Motor Excitant.)

℞ 10.

Tincture of Digitalis	30 cc.
Isoalcoholic Elixir, *q. s.*	120 cc.

Sig: Teaspoonful in water three times daily after meals. (Cardiant.)

Important. A complete revision of the regulations governing the importers, manufacturers wholesalers and retailers licensed under the Harrison Narcotic Act and other Federal narcotic laws has been prepared by the Bureau of Narcotics, U. S. Department of the Treasury. It is expected that copies of the revised regulations will be made available, during July or August, to the Deputy Collectors of Internal Revenue for distribution to every registrant. A codification of these regulations became necessary under Act of Congress requiring a codification of all regulations under Federal Acts. It was thought advisable to bring them completely up-to-date at the same time and this explains the revision.

NOTICE TO CONTRIBUTORS TO THE JOURNAL AMERICAN PHARMACEUTICAL ASSOCIATION.

The following notice has been prepared from comments received from members of the Board of Review of Papers and of the Publication Committee.

Manuscripts should be sent to Editor E. G. Eberle, 2215 Constitution Ave., N. W., Washington, D. C.

All manuscripts should be typewritten in double spacing on one side of paper $8^1/_2$ x 11 inches, and should be mailed in a flat package—not rolled. The original (*not* carbon) copy should be sent. The original drawings, not photographs of drawings, should accompany the manuscript. Authors should indicate on the manuscript the approximate position of text figures. All drawings should be marked with the author's name and address.

A condensed title running page headline, not to exceed thirty-five letters, should be given on a separate sheet and placed at the beginning of each article.

The method of stating the laboratory in which the work is done should be uniform and placed as a footnote at end of first page, giving Department, School or College. The date when received for publication should be given.

Numerals are used for figures for all definite weights, measurements, percentages, and degrees of temperature (for example: 2 Kg., 1 inch, 20.5 cc., 300° C.). Spell out all indefinite and approximate periods of time and other numerals which are used in a general manner (for example: one hundred years ago, about two and one-half hours, seven times).

Standard abbreviations should be used whenever weights and measures are given in the metric system, *e. g.*, 10 Kg., 2.25 cc., etc. The forms to be used are: cc., Kg., mg., mm., L. and M.

Figures should be numbered from 1 up, beginning with the text-figures (line engravings are always treated as text-figures and should be designed as such) and continuing through the plates. The reduction desired should be clearly indicated on the margin of the drawing. All drawings should be made with India ink, preferably on white tracing paper or cloth. If coördinate paper is used, a blue-lined paper must be chosen. Usually it is desirable to ink in the large squares so that the curves can be more easily read. Lettering should be plain and large enough to reproduce well when the drawing is reduced to the width of a printed page (usually about 4 inches). Photographs intended for half-tone reproduction should be securely mounted with colorless paste.

"Figure" should be spelled out at the beginning of a sentence; elsewhere it is abbreviated to "Fig.;" per cent—2 words.

The expense for a limited number of figures and plates will be borne by the JOURNAL; expense for cuts in excess of this number must be defrayed by the author.

References to the literature cited should be grouped at the end of the manuscript under the *References*. The citations should be numbered consecutively in the order of their appearance (their location in the text should be indicated by full-sized figures included in parentheses). The sequence followed in the citations should be: Author's name (with initials), name of publication, volume number, page number and the date in parentheses. Abbreviations for journals should conform to the style of *Chemical Abstracts*, published by the American Chemical Society.

(1) Author, A. Y., *Am. J. Physiol.*, 79, 289 (1927).

Papers presented at the Sections of the AMERICAN PHARMACEUTICAL ASSOCIATION's annual meeting become the property of the Association and may at the discretion of the Editor be published in the JOURNAL. Papers presented at these Sections may be published in other periodicals only after the release of the papers by the Board of Review of Papers of the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

The Editor will appreciate comments from Board of Review and Committee on Publication, members, authors and others interested.

NEW ZEALAND PHARMACIES.

New Zealand has taken steps, under the pharmacy reorganization plan to ultimately limit the number of pharmacies on the basis of population; and to redistribute, so far as possible, the existing pharmacies, with the object of providing a more adequate service to the public. Pharmacies will operate on a strict license and under a uniform scale of charges for dispensing medicines.

PROCEEDINGS OF THE LOCAL BRANCHES

MICHIGAN.

The Seventh Annual Pharmaceutical Conference, sponsored by the University of Michigan, College of Pharmacy, in conjunction with the Michigan Branch, A. PH. A., was held on May 18, 1938, and was most successful. When Dr. Howard B. Lewis, director of the College of Pharmacy and chairman of the Conference, called the session to order an overflow gathering of pharmacists, students and scientists was assembled, numbering three hundred or more, the largest attendance in the history of these conferences, giving much encouragement to the members interested in the advancement of the profession. Dr. Lewis introduced Dr. Clarence S. Yoakum, vice-president of the University and dean of the Graduate School, who welcomed the conference members to the University and encouraged them to make use of the many facilities offered by the University of Michigan.

"What Should Be the Objective of a Modern Pharmacy Act?" was the subject presented by the first speaker of the conference, Dr. Robert L. Swain, secretary of the Maryland State Board of Pharmacy and president of the National Association Boards of Pharmacy. Dr. Swain said that rigid regulation of the manufacture of pharmaceuticals, patent medicines and proprietaries is as necessary for the public interest and protection as the supervision of the retail drug store. He insisted that the State Board of Pharmacy should be empowered to issue or refuse permits to manufacturer and wholesale distributor, supervise personnel and inspect factory conditions as well as interest itself in the technical education and in the individual pharmacist. Discussion followed by Otis F. Cook, R. L. McCabe, Dean R. T. Lahey and others. Dr. Swain also brought to the Conference the greetings of President E. N. Gathercoal, of the AMERICAN PHARMACEUTICAL ASSOCIATION, and Secretary E. F. Kelly.

"The Use and Abuse of Sulfanilamide" was the next subject on the Program and was ably presented by Dr. Arthur C. Curtis, Associate Professor of Medicine, University of Michigan. Dr. Curtis clearly outlined the uses of this drug and condemned the cure-all claims for it. However, he recommended its use in many cases where clinical tests have proved Sulfanilamide invaluable. He, however, suggested the careful observation of the patient during the administration of this drug.

Professor Clifford C. Glover, Professor of Pharmacognosy, University of Michigan, was the next speaker and presented a most timely and much discussed topic, "The Marihuana Problem." Professor Glover gave a very complete history of the weed and the uses it has been put to and the many abuses which have been made of the drug. The many pathetic cases illustrated by Professor Glover through the abuse and illegitimate use of the drug clearly demonstrated the necessity for the Marihuana Act.

This brought to a close the afternoon session of the Conference.

After dinner the assembly adjourned to the Chemistry Building of the University of Michigan where the meeting of the Michigan Branch, A. PH. A., was called to order by President Earl Soop. The minutes of the previous meeting were read by the secretary and approved.

Dr. Leonard A. Seltzer, chairman of the Nominating Committee, then made a report which was accepted, and it was moved by John H. Webster that the secretary cast a unanimous ballot for the election of the officers as presented by the Committee, which was done.

President Earl Soop then introduced the speaker of the evening, Dr. Allan J. McLaughlin, Lecturer in Hygiene and Public Health, University of Michigan, also former Surgeon General of the United States Public Health Service. Dr. McLaughlin presented a most interesting paper on the "Outlook for the Control of Communicable Disease." Some of the results attained are astounding and encouraging; for example, tuberculosis has been reduced from 300 to 60 per 100,000. Dr. McLaughlin explained this is partly due to the better standards of living. However, much credit must be given to the education and public health service and Red Cross campaigns to stamp out this dread plague. Lobar pneumonia which was hopeless in 1916, to-day can be checked, and in many cases the life of the patient can be saved by the use of vaccine developed. However, Dr. McLaughlin made it clear that the proper type of vaccine to fit the individual is absolutely necessary to bring about recovery in pneumonia. In the rural centers he said the nurse is responsible for 11,000 people, that is the ratio as it is to-day. Dr. McLaughlin said the need

for larger funds to carry on this great work by the nurse is absolutely necessary particularly in caring for the children of the rural centers.

Mr. Webster commented on the splendid talk by Dr. McLaughlin and expressed the interest the pharmacist holds in public health and the responsibility held by this group.

Mr. Leonard A. Seltzer suggested a rising vote of thanks to the speaker and to the faculty of the College of Pharmacy of the University of Michigan for their hospitality, making the day most enjoyable and one to be remembered by the members attending the Conference.

This brought to a close a most successful year for the Michigan Branch, A. PH. A., and the outlook for 1939 is exceedingly bright with the hope of being able to entertain the convention of the A. PH. A. in Detroit.

BERNARD A. BIALK, *Secretary.*

Midwestern small city families are more likely to economize by not seeing the dentist, the oculist—or even the doctor—than by not buying supplies for the family medicine chest, when funds run low, as is indicated in a table of medical expenditures for 3118 native white non-relief families, including husband and wife, both born in this country, and living in seven representative cities: Lincoln, Ill.; Boone, Iowa; Columbia and Moberly, Mo.; Mount Vernon and New Philadelphia, Ohio; and Beaver Dam, Wis. The table is a part of a nation-wide study of how much money the American family makes and how it is spent, conducted under the direction of Dr. Louise Stanley, chief of the Bureau of Home Economics, U. S. Department of Agriculture.

Income for the year reached the $500.00 level before as many as half the families reported expenditures for a physician; $1250–$1499, before that number consulted the dentist; and $4000–$4999 before one family in four paid an oculist fee; but a majority of families at all income levels (67 to 92 per cent) reported expenditures for medicines and drugs during the twelve-month period studied in 1935–1936, averaging $6.00 to $21.00 per family, including those that made no purchases.

In the lowest income class studied, $250.00–$499.00, less than 40 per cent of the families spent money for doctor's fees; less than 12 per cent for dentist's services; none for oculist's services; and 67 per cent for medicines. In the second lowest income class, $500.00–$750.00, approximately 50 per cent of the families had expense for the physician; 25 per cent for the dentist; less than half of one per cent for the oculist; 75 per cent for medicines. At the highest income level studied, $5000–$10,000, only 75 per cent of the families reported expense for a physician; 80 per cent for the dentist; less than 25 per cent for an oculist; and 92 per cent for medicines.

Five per cent of the families in the lowest income class ranging to 24 in the highest, averaging from $3.00–$21.00, were next to the highest. Although the percentage of families having such expenses increased with income, families with the very least to spend were not exempt. The number of families paying health and accident insurance premiums, in one income class, $2250–$2499, was approximately twice as large as the number paying hospital bills; the percentage of families making such payments ranging from 12 in the lowest class to 44 in the highest. These premiums took an average of $2.00 per family based on all families in the lowest income class, $250.00–$499.00, and $27.00 in the highest.

Of income levels above $500.00, 90 to 99 per cent of families had some expense for medication with differences in average amounts at the different income levels; between $250.00 and $500.00, the average for all families was $28.00 for the year or about $2.00 a month, while between $5000 and $10,000 the average was $184.00, or about $15.00 a month. With incomes between $1000 and $1250, 467 families averaged $47.00 during the year for medical care, as follows: physician, $14.00; dentist, $6.00; oculist, $1.00; medicine and drugs, $6.00; hospitalization, $5.00; health and accident insurance premiums, $6.00; and all other items including other specialists, clinic visits, nursing service, etc., $9.00. With incomes between $2000 and $2249, 215 families averaged $77.00; physician, $20.00; dentist, $11.00; oculist, $1.00; medicine and drugs, $8.00; hospitalization, $8.00; health and accident insurance, $16.00; and other items, $13.00. With incomes between $3000 and $4000, 201 families averaged $114.00; physician, $23.00; dentist, $20.00; oculist, $2.00; drugs and medicines, $14.00; hospitalization, $17.00; health and accident insurance, $21.00; other items, $17.00. With incomes between $5000 and $10,000, families averaged $184.00; physician, $32.00; dentist, $26.00; oculist, $3.00; drugs and medicines, $21.00; hospitalization, $15.00; health and accident insurance, $27.00; other items, $60.00.

ASSOCIATION BUSINESS

AD INTERIM BUSINESS OF THE COUNCIL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, 1937–1938.

Office of the Secretary, 2215 Constitution Ave, Washington, D. C.

LETTER NO. 9.

May 27, 1938.

To the Members of the Council:

A vote is called for on Motions Nos. 20, 21 and 22 as submitted in Council Letter No. 8.

55. Use of Text of N. F. VI. The following communication has been received from Chairman DuMez of the Committee on Publications:

> "In response to the request of the Council on Dental Therapeutics, it is recommended that that organization be granted permission to use portions of the text of the N. F. VI, without the payment of the usual fee, in the coming annual revision of Accepted Dental Remedies."

(*Motion No. 23*) It is moved by DuMez that the Council on Dental Therapeutics of the American Dental Association be granted permission to use portions of the text of the N. F. VI in a forthcoming edition of Accepted Dental Remedies with the usual acknowledgment, and for value received.

56. Applicants for Membership: The following applications, properly endorsed and accompanied by the first year's dues, have been received:

No. 380, A. J. Affleck, 1008 10th St., Sacramento, Calif.; No. 381, Sister Jane Frances Byrne, 812 Adams St., Montgomery, Ala.; No. 382, George B. Boyd, Monticello, Minn.; No. 383, Hallie Frances Bruce, U. of Minn. Hospital, Minneapolis, Minn.; No. 384, Sister Mary Tekakwitha Jump, St. Patrick Hospital, Missoula, Mont.; No. 385, J. K. Haynie, 121 So. 8th St., Opelika, Ala.; No. 386, Benjamin Schultz, 200 W. 16th St., New York, N. Y.; No. 387, Dorothea F. Stoner, 1044 N. Francisco, Chicago, Ill.; No. 388, Earl H. Frasier, Box 207, Pedro Miguel, Panama Canal Zone; No. 389, Anthony C. Nitti, 110 Skillman Ave., Brooklyn, N. Y.; No. 390, Robert E. Evans, Meadow Grove, Nebr.; No. 391, H. L. Bellamy, Cambridge, Nebr.; No. 392, Frank L. Mercer, 4619 Nebraska, St. Louis, Mo.

(*Motion No. 24*) Vote on applications for membership in the ASSOCIATION.

E. F. KELLY, *Secretary*.

LETTER NO. 10.

June 10, 1938.

To the Members of the Council:

57. Use of Text of N. F. VI. Motions No. 20 (Council Letter No. 8, page 439) and No. 23 (Council Letter No. 9, page 526) have been carried and appropriate notices have been forwarded.

58. A. Ph. A. Laboratory. Motion 21 (Council Letter No. 8, page 442) has been carried and the Rules for the Supervision of the Laboratory are approved as submitted, and the persons named are declared elected as members of the permanent Committee on Laboratory to serve as indicated.

59. Election of Members. Motions No. 22 (Council Letter No. 8, page 439) and No. 23 (Council Letter No. 9, page 526) have been carried and applicants for membership numbered 339 to 392, inclusive, are declared elected.

60. Change in Name of the Detroit Branch. The following is quoted from a letter received from Secretary Bernard A. Bialk for the information of the members of the Council: "Please be advised of the action taken officially by the Branch in changing of the name it has been known by for twenty-five years. At the April meeting, on motion of Mr. R. L. McCabe, the name of the Branch was officially changed from the Detroit Branch to the Michigan Branch of the AMERICAN

PHARMACEUTICAL ASSOCIATION. The proceedings of the April meeting, which you have at hand, contain the action taken on the change."

61. Tentative General Program of the Minneapolis Meeting. Local Secretary Rogers, with the approval of the Local Committee on Arrangements, and the Committee on General Program, submit the tentative program as attached to this letter. (See page 449.) The management of the Hotel Nicollet has approved the assignment of meeting rooms. It may be necessary to make minor changes in the tentative program as submitted and if so, the Council will be advised. In general arrangement, the program follows that for the New York meeting.

(*Motion No. 25*) It is moved by Kelly that the Tentative General Program of the Minneapolis Meeting be approved as submitted.

62. Applicants for Membership. The following applications, properly endorsed and accompanied by the first year's dues, have been received:

No. 393, Lawrence A. Schulz, 917 N. Milwaukee St., Milwaukee, Wis.; No. 394, Irving H. Simonson, 61 Main St., Marathon, Wis.; No. 395, Peter J. Hauper, Union Grove, Wis.; No. 396, Julius Segal, 14th & Washington Sts., Wilmington, Del.; No. 397, Margaret Airston, Univ. of Southern California, Los Angeles, Calif.; No. 398, James F. Robinson, 6 E. Broadway, Salt Lake City, Utah; No. 399, A. Roy F. Johnson, 1600 W. Lake St., Minneapolis, Minn.; No. 400, Eugene Schaeffer, Riverside Drive 150, New York, N. Y.; No. 401, Albert R. Strafella, Paris Road, New Hartford, N. Y.; No. 402, James D. Sloan, Jr., 4 Ball St., Hoosick Falls, N. Y.; No. 403, Benjamin M. McBride, 7033 Prospect, Kansas City, Mo.; No. 404, Adolph Schulman, 965 44th St., Brooklyn, N. Y.; No. 405, Anna M. Danielson, 2339 Central N. E., Minneapolis, Minn.; No. 406, Harry M. Fletcher, 1409 Willow St., Minneapolis, Minn.; No. 407, Keith K. Keller, Bloomington and Lake Sts., Minneapolis, Minn.; No. 408, Marie A. Piesinger, Northfield, Minn.; No. 409, John B. Tomhave, 215 No. First St., Montevideo, Minn.; No. 410, Fred J. Hersh, 4626-28 W. Burleigh, Milwaukee, Wis.

(*Motion No. 26*) Vote on applications for membership in the ASSOCIATION.

E. F. KELLY, *Secretary.*

INTERNATIONAL PHARMACEUTICAL FEDERATION.

LEYDEN, HOLLAND.

To the Presidents of the National and Affiliated Associations.

Sirs:

In a meeting of the Bureau which met May 18th, there was discussed the question of very intensive international collaboration. As you know, there exists an understanding between the many countries for the exchange of pharmacists who desire to study practical pharmacy in another country.

The Bureau hopes that it will be possible to make, in a short time, some plans concerning international courses to be given by professors and other competent speakers. These propositions will be placed before the next General Assembly.

During the discussion we learned that one does not know yet what center of documentation has been formed in the general secretaryship of the Federation, and it is above all to draw your attention to this that we address ourselves at this moment to the Presidents of the Associations.

The Federation has her friends in all the countries of the world, and when you yourself, or one of your members, desire to contact foreign brothers, it is sufficient to turn to the General Secretary of the Federation, who can give very often the necessary information. In many instances when a member of a National association desires to have an introduction to the laboratories in certain countries, the General Secretary has been able to introduce those colleagues among the indicated institutions.

We hope you will draw the attention of your member, whether professional or scientific, to this work. On the other hand, we hope that the Bureau of our Association will give you all useful information and all the help of which you will have need, and that you have always secured the assistance of the national secretaries, when you have consulted them.

Receive, Mr. Presidents, our devoted sentiments.

For the Bureau of the Federation,

E. HÖST MADSEN, *President.*
T. POTJEWIJD, *General Secretary.*

EDITORIAL NOTES

A. PH. A. MEMBERSHIP PRIZES.

The following have received one year's membership in the A. PH. A., as a prize for excellence in various studies:

Fred J. Kirchmeyer, St. Louis College of Pharmacy, for excellence in the past year's work.

Woodrow Wilson Webb, University of Illinois, Chicago, Ill., the William Gray Prize.

Robert N. Watson, University of North Carolina, Chapel Hill, N. Car., the Henry M. Burlage Prize, for excellence in Pharmaceutical subjects.

William L. Vollmer, Louisville College of Pharmacy, the Gordon L. Curry Prize, for greatest improvement in four-year course.

Walter Peregon, Wayne University, Detroit, Michigan, Faculty Award for second highest scholarship rating in graduating class.

Sister M. Sylvester Evan, Duquesne University, Pittsburgh, Pa., Department of Materia Medica, offered by Dr. Elbert Voss.

Harry F. Kennedy, Duquesne University, Pittsburgh, Pa., offered by Dean H. C. Muldoon, for excellence in Chemistry.

Victor L. Zuchowski, Duquesne University, Pittsburgh, Pa., offered by Professor Ralph B. Kreuer, for excellence in Pharmacy.

Robert D. Merchant, Massachusetts College of Pharmacy, by Prof. E. V. Lynn, for excellence in Analytical Chemistry.

Warren K. Macurdy, Massachusetts College of Pharmacy, by Prof. L. A. Thompson, for excellence in Pharmacy.

Norman R. Lacombe, Massachusetts College of Pharmacy, by Prof. W. H. Glover, for excellence in Materia Medica.

Jonas H. Bond, Massachusetts College of Pharmacy, by Prof. Irving P. Gammon, for excellence in Organic Chemistry.

Robert F. Larsen, Massachusetts College of Pharmacy, by Prof. Leon C. Ellis, for excellence in Business Administration.

Benjamin M. McBride, Kansas City College of Pharmacy, by Dean D. V. Whitney, for scholarship.

Adolph Schulman, Brooklyn College of Pharmacy, for scholarship.

Laura Bell Gaulding, The Women's Organization of the Memphis Drug Club, Memphis, Tennessee, for scholarship.

NEW JERSEY BOARD OF PHARMACY.

In the future the Board of Pharmacy will be guided by the following resolution in issuing permits to establishments not owned and operated by registered pharmacists:

WHEREAS, Surveys and available statistics gathered by the Board of Pharmacy of the State of New Jersey indicate clearly that the number of permits which have been issued for the operation of pharmacies and drug stores in this state is entirely adequate to meet the requirements of the public for necessary prescription services and other pharmaceutical needs, and

WHEREAS, There is a tendency on the part of corporations not owned by registered pharmacists of the State of New Jersey to add units to their chains of pharmacies and drug stores already in operation in the State of New Jersey, and

WHEREAS, The policy of these business interests engaged in multiplying the number of pharmacies or drug stores is largely one of using the permit to conduct a pharmacy or drug store as a cloak for carrying on unrelated merchandising activities, which may tend to reduce the availability of professional services now rendered by pharmacists, be it

Resolved, That the Board of Pharmacy of the State of New Jersey shall hereafter refuse to grant permits for the operation of pharmacies or drug stores in the State of New Jersey to individuals who are not registered pharmacists in the State of New Jersey and to corporations which are not owned and operated by pharmacists registered in the State of New Jersey, unless it can be shown that the issuance of permits to such organizations is a necessity from the standpoint of public health and welfare, and be it further

Resolved, That proper steps be taken to acquaint the people of New Jersey with the following facts:

1. That this action of the Board is not taken for the purpose of creating a monopoly for registered pharmacists, because it does not prevent persons who have qualified as pharmacists by examination and registration from engaging in open competition with other pharmacists in the field of service for which they have qualified.

2. That this action has been taken to limit or prevent, if possible, the destructive tactics of operators of so-called "cut rate" and "pine

board" stores whose principal objective is to demoralize and drive out of business existing pharmacies owned and operated by pharmacists legally qualified and ably supplying adequate professional services, thus creating an eventual monopoly of the practice of pharmacy by business interests which have no professional background and are interested solely in the financial returns from commerce in drugs and medicines.

3. That this resolution does not affect pharmacies or drug stores for which permits have already been issued and which are in actual operation at the time these resolutions are passed.

MEDICAL COLLEGE OF VIRGINIA.

The Centennial and Commencement exercises of the Medical College of Virginia were held June 4th to 7th. The sermon was given by Dr. Beverley D. Tucker, in historic St. Paul's Church, on the night of June 5th.

On Tuesday morning, June 7th, the Centennial exercises proper were held. Greetings were extended by representatives of the State and City, the Founding College and others. Dr. Forest R. Moulton, Permanent Secretary of the American Association for the Advancement of Science, brought greetings in the name of science. Dr. Henry A. Christian, Hersey Professor of the Theory and Practice of Physics, Harvard Medical School, made the principal address of the day, his subject being "The Lure of Medicine." More than one hundred thirty delegates from various colleges, universities, State and National organizations attended the exercises.

Commencement exercises were held on the night of June 7th, one hundred thirty-nine young men and women receiving degrees in the four schools of Medicine, Dentistry, Pharmacy and Nursing. President J. Rion McKissick of the University of South Carolina delivered the address.

The honorary degree of Doctor of Science was conferred upon Dr. James Carroll Flippin, Dean, Department of Medicine, University of Virginia, at the final exercises.

Dr. E. F. Kelly represented the A. PH. A. on this occasion.

The Indiana Pharmaceutical Association convention at French Lick Springs, June 21st to 23rd, was well attended. Nationally known speakers, as well as Indiana retailers and wholesalers, presented outstanding talks on various phases of the retail drug industry. Dr. Neal Bowman, Temple University, Philadelphia, delivered an address on "A B C's of Selling;" Louis V. Eytinge, Royal Manufacturing Company of Duquesne, Chicago, stressed the benefits to be derived from "Determination;" Dr. K. K. Chen spoke on "Digitalis-Like Drugs Since the Time of William Withering." Fair Trade problems were discussed by A. C. Fritz, secretary of the Indianapolis Drug Club.

RUDOLPH MATAS RECEIVES DISTINGUISHED SERVICE MEDAL.

The first medal for distinguished service to scientific medicine to be awarded by the American Medical Association was given to Rudolph Matas, surgeon, of New Orleans, by the House of Delegates in the election held June 13th. The recipient of this medal is chosen by a process of selection which insures choice of an outstanding physician and scientist.

The first College of Pharmacy in the United States was founded in 1821, one hundred and seventeen years ago. During the following fifty years the number of pharmacy schools had increased to a total of eleven. All of these except one were located in large cities and were convenient for the druggists' apprentices in the cities in which they were. It was a long time before others than apprentices were attracted as matriculants in the courses in pharmacy. The University of Michigan in 1868, offered instruction in pharmacy as a part of the university curricula. This was the beginning of pharmacy colleges in state universities. To-day more than one-half of our pharmacy colleges and schools have university and college connection and state support.

In the seventies, eighties and nineties there was a marked growth in the number of colleges of pharmacy established at the state universities. This was true chiefly of those states east of the Appalachian Mountains. At about this same time laws regulating the practice of pharmacy were enacted by many states. Boards of Pharmacy likewise came into being in rapid succession.

The pharmacist of the future is bound to be an educated man. He will know pharmacy and appreciate its traditions. Furthermore, he will know why he is a pharmacist, and why people want his services. He will be a better scientist and a great humanitarian. He will be informed in the arts and be classed as a cultured person.

PERSONAL AND NEWS ITEMS.

California Pharmaceutical Association met in convention Sunday evening, June 19th, at Oakland. A large body of druggists was registered, and the meeting was a very helpful one.

The Maryland Pharmaceutical Association met in Baltimore, Md., Lord Baltimore Hotel, on June 21st–23rd. The convention was well attended and much good was accomplished.

Idaho Pharmaceutical Association met in Lewiston, June 20th–22nd, at the Lewis-Clark Hotel. Lewiston is a wonderful convention city, and a most interesting program was enjoyed.

The Committee to Revitalize the D. C. Pharmaceutical Association held a luncheon meeting in the Raleigh Hotel, on June 30th. A large number of members and officers was present.

Congress has passed a bill authorizing the construction of a new building for the Army Medical Library and Museum. At last the world's mightiest collection of medical literature and one of the largest of medical museums will be given adequate quarters.

An act has been signed by the President creating the Saratoga National Historial Park in New York. The center of this park will be a section of the battlefield of Saratoga.

The House of Representatives passed a bill establishing the Olympic National Park in northwestern Washington.

Colonel Marston T. Bogert, of Columbia University, is the recipient of the Priestley Medal in recognition of his splendid services to science.

Mr. Frank L. McCartney has been made president of the Norwich Pharmacal Co.

At its meeting in April, held at the Nicollet Hotel in Minneapolis, the Minnesota State Pharmaceutical Association passed a resolution that in any hospital rendering a pharmaceutical service, that service should be under the supervision of a registered pharmacist. A similar resolution to this was passed at the meeting of the Fifth District of the National Association Boards of Pharmacy which was held in Des Moines, April 3rd and 4th.

The requirements of the American Medical Association and of the American College of Surgeons was referred to in an editorial in the October 1937, issue of the JOURNAL.

The University of Buffalo granted twenty-two degrees of Graduate in Pharmacy, and three degrees of Bachelor of Science in Pharmacy, at its 92nd commencement, recently. Three senior students received honors.

Dr. Melvin W. Green, of the Mellon Institute of Industrial Research, has accepted an assistant professorship of Biochemistry at the Cincinnati College of Pharmacy, the oldest institution of its kind west of the Allegheny mountains.

For the past two years Dr. Green has been working on the revision of the monographs for the organic chemicals of the United States Pharmacopœia, under the direction of Dr. George D. Beal. Prior to his connection with the Mellon Institute, Dr. Green served as Parke, Davis & Co. Graduate Fellow on Cascara Research at the University of Pittsburgh, from which institution he received the Doctor of Philosophy degree in Chemistry.

Dr. Green, who is president-elect of the Pittsburgh Branch, A. PH. A., and is quite active in local Chemical organizations, just announced his engagement to Miss Mary Hostler, also a chemist at the Mellon Institute. The wedding will take place probably late in the summer.

The Connecticut Pharmaceutical Association met in New London, June 15th and 16th. Some very interesting papers were read, and altogether a most successful meeting was held.

West Virginia Pharmaceutical Association met in Charleston, June 19th to 21st. The importance of Fair Trade was stressed by President Flesher and Secretary Hayman. Dr. George A. Moulton, president of the New Hampshire Pharmaceutical Association, explained the "New Hampshire Plan," and also spoke on "Ramifications to Fair Trade." Dr. Frank B. Kirby, of Abbott Laboratories, delivered a masterful address on "What the Retail Druggist Should Know about Vitamins." Mr. O. J. McClure delivered an interesting address on "Salesmanship."

The American Chemical Society will meet in Milwaukee, Wis., on September 5th to 9th.

Next year the spring meeting will be held in Baltimore, Md., and the fall meeting in Boston, Mass. In 1940 the spring meeting will be held in Cincinnati, Ohio.

Mr. P. H. Costello, of Cooperstown, N. D., secretary of the North Dakota Board of Pharmacy and former president of the A. PH. A., was a victor in the recent four-cornered mayoralty race, there.

Dr. C. Leonard O'Connell, dean of the College of Pharmacy, University of Pittsburgh, has been named president of the Civic Club of Allegheny County.

More than three hundred alumni attending the annual reunion banquet of the Albany College of Pharmacy, in the Colonie Country Club were present at the dedication of the Throop Drug Store, from Schoharie County, installed as a drug store museum in memory of the late Professor Edwin C. Hutman.

At the convention of the Colorado Pharmaceutical Association held June 7th to 9th, **Mr. W. Mac Childs,** first vice-president of the A. PH. A., spoke on "Interprofessional Relations."

The Michigan Pharmaceutical Association plans to publish a magazine within the next few months. This action was taken at the convention held on June 7th to 9th, in Lansing.

The North Dakota Pharmaceutical Association was held in Mandan recently, in the World War Memorial Building. At this meeting druggists were urged to read more of their weekly and monthly trade publications. Convention speakers included: Dr. Neal Bowman, Commercial Pharmacy, Temple University, Philadelphia, Pa.; Dr. Culver S. Ladd, State Food Chemist, Bismarck; Dr. J. O. Arnson, Bismarck, who represented the North Dakota Medical Association; and Dean W. F. Sudro, School of Pharmacy, North Dakota State College, Fargo.

The Mississippi Pharmaceutical Association recently held its convention in Gulfport. At this meeting the State Fair Trade set-up was completed, under direction of Secretary S. B. Key. The association joined with the Georgia Association in inviting the AMERICAN PHARMACEUTICAL ASSOCIATION to hold its 1939 convention in Atlanta. This year's convention was voted one of the biggest and most successful Mississippi meetings.

The Arkansas Pharmaceutical Association in convention at Hot Springs demanded that a School of Pharmacy be established at the University of Arkansas. Retailers declare there is a shortage of pharmacists and that the pharmacy school is needed immediately. Roger M. Martin, retiring president, reported business conditions throughout the state "generally good."

Kentucky Pharmaceutical Association met recently in Middlesboro. The progress of Pharmacy in Kentucky was lauded. J. W. Gayle, seventy-eight years of age, was elected to serve his fiftieth term as secretary of the Association.

At the Pennsylvania Pharmaceutical Association convention held recently, coöperation between the physicians and pharmacists of Pennsylvania was urged. Dr. E. J. Bishop, president of the Pennsylvania State Medical Association, outlined the plan developed by the AMERICAN PHARMACEUTICAL ASSOCIATION in coöperation with the American Medical Association. J. B. Pilchard, Harrisburg, who has been secretary of the Association for nine years resigned, due to the fact that he has recently gone into business.

Michigan Pharmaceutical Association met in Lansing recently. Complete revision of Michigan's pharmacy act during the next session of the state legislature was seen as a probability due to action taken at this convention. Chairman of the Fair Trade Committee, Dan W. Houser, of Detroit, stated that the Fair Trade Law is returning sales to the independent druggists.

Colonel Charles A. Lindbergh will devote his time to Science and his studies will be conducted largely with Dr. Alexis Carrel. Ultimately Dr. Carrel hopes the artificial heart will develop into a fountain of information in studying the food requirements of body tissues. There are many developments which will more and more interest the pharmacist.

Under the recently enacted H. J. Resolution 683, any retail pharmacist who has on hand as of July 1, 1938, any tax paid ethyl alcohol or other distilled spirits intended for non-beverage use, must make an inventory and file it with a return on Treasury Form 758, in triplicate, on or before July 31, 1938. This regulation applies whether the pharmacist holds a retail liquor dealer's license or not.

OBITUARY.

MACOMB G. FOSTER.

Mr. Macomb G. Foster, vice-president of Fairchild Brothers & Foster, and former president of Knickerbocker Hospital, died unexpectedly on June 1st. Mr. Foster was 78 years of age and had been with Fairchild Brothers & Foster for fifty-seven years. He was a native of New York City, and the son of the late William Foster, Jr., and Caroline Macomb Foster. He received his early education in New York and Connecticut.

When Mr. Foster became president of Knickerbocker Hospital in 1919 he had already been a trustee for twenty-three years. In his forty-nine years' association with the hospital he had participated in all fund-raising campaigns and in 1924 broke the ground for the institution's emergency building at 131st St. and Convent Avenue.

Mr. Foster was a member of the Century Association, the Scawannaka Corinthian Yacht Club, the Quill Club and the New England Society. He was also a vestryman of St. Matthew's and St. Timothy's Protestant Episcopal Church, where funeral services were held.

Mrs. Foster, the former Annie Garnett, of Richmond, Va., died in 1933. A brother, Pell William Foster, of New York and Tucson, Ariz., survives.

ROYAL S. COPELAND.

Dr. Royal S. Copeland was born in Detroit, Mich., in 1868, graduated from the Medical School of the University of Michigan in 1889, and after taking graduate courses abroad settled in Bay City, Mich. He was Professor of Ophthalmology in his Alma Mater from 1895 to 1908, when he went to New York City as Professor of Ophthalmology in the New York Homeopathic Medical College and Flower Hospital. Mayor Harlan appointed Dr. Copeland Commissioner of Public Health and president of the Board of Health of New York City in 1918, which position he held until his election as Senator from New York in 1922. He was reëlected in 1928 and again in 1934.

During his residence in Ann Arbor, Dr. Copeland served as Mayor of the City and as Chairman of the Board of Education. The protection and improvement of public health had Dr. Copeland's enthusiastic and effective support during his long professional and public career and he was early recognized as a leader in his chosen field.

Reference only can be made here to his sponsorship of Food, Drug and Cosmetic legislation in Congress from 1933 to its enactment only a few days before his death. Although he refused to compromise on principles he kept an open mind and was always willing to consider criticism and suggestion. As Secretary of Agriculture Wallace said, "The Act will stand as a legislative monument to the memory of the late Senator Royal S. Copeland who fought for a really effective measure throughout the five-year struggle over revision of the Act of 1906."

There is every reason to believe that those who are being graduated in pharmacy to-day know much more about it than those who practiced it in the so-called "good old days." Pharmacy as a science and a field of service finds anchorage in many basic sciences. Its practice permits those in it to make use of a vast store of knowledge. In addition to knowing a great deal about pharmacy and drugs, the modern pharmacist needs to be highly trained in chemistry and the biological sciences. These latter fields are growing and expanding so rapidly that only the expert can know all the changes. The pharmacist, as no other professional man, places himself at the services of an inquiring and demanding public. It is only reasonable that he should be the best informed man in the community upon all things pertaining to medicines both new and old. The public expects much of the pharmacist. It will expect more than ever of the future pharmacist and he cannot fail them.

The future pharmacist will choose his profession because of the splendid opportunities for service which it will offer. In the past most students have endured the course in pharmacy as a means to a business enterprise. In the future the course will be chosen because of its historical and informational value. For these reasons alone it has a great appeal. In addition it affords the opportunity for doing a specialized technical service. The service motive makes an appeal which is vastly different from that of merchandising. Young men who are uninterested in the professional aspect of pharmacy will be discouraged and directed to choose other fields. When this becomes the rule, there will be no reason to question pharmacy's claims to professionalism.